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JANUARY 1952. No. 1

Fat Embolism. A Problem in the Differential Diagnosis of Craniocerebral Trauma. RICHARD C. SCHNEIDER 1

A Study of the Causes of Failure in the Herniated Intervertebral Disc Operation. An Analysis of Sixty-Seven Reoperated Cases. JAMES GREENWOOD, JR., T. H. MCGUIRE, and FARISS KIMBELL 15

Procaine Block of Frontal Lobe White Fibers as a Means of Predicting the Effect of Prefrontal Lobotomy. I. Experimental Studies. ORVILLE T. BAILEY, WILFRED T. SMALL, and FRANC D. INGRAHAM. With an Introductory Note by WILLIAM P. VAN WAGENEN. 21

Procaine Block of Frontal Lobe White Fibers as a Means of Predicting the Effect of Prefrontal Lobotomy. II. Clinical Evaluation. WILLIAM P. VAN WAGENEN, and C. T. LIU 30

Recovery from the Decerebrate State Associated with Supratentorial Space-Taking Lesions. HOWARD FREEDMAN 52

Hydrocephalus from Overproduction of Cerebrospinal Fluid (and Experiences with Other Papillomas of the Choroid Plexus). EDGAR A. KAHN, and JOHN T. LUROS 59

The Effects of Intracarotid Diodrast. ELDON L. FOLTZ, L. B. THOMAS, and A. A. WARD, JR 68

Tissue Reactions to Powdered Tantalum in the Central Nervous System. ORVILLE T. BAILEY, FRANC D. INGRAHAM, PRESTON S. WEADON, and ANTHONY F. SUSEN 83

CASE REPORTS AND TECHNICAL NOTES:

Myelographic Diagnosis of Sacral Perineurial Cyst. Z. EDIN TAHERI, PAUL RIEMENSCHNEIDER, and ARTHUR ECKER 93

Pyogenic Subdural Abscess of the Spinal Meninges. Report of Two Cases. JUAN NEGRIN, JR., and ROBERT A. CLARK, JR. 95

Tantalum Cranioplasty and Repeated Trauma. OSCAR A. TURNER. 100

The Lucite Calvarium. A Case Report. GALE CLARK 103

A Simple Radio-Opaque Screen for Angiography. GORDON L. SMILEY 107

A Simple Device for Position Determination During Myelography. I. MELBOURNE GREENBERG 108

NOTICES 111

MARCH 1952. No. 2

Alfred Washington Adson—Pioneer Neurosurgeon. 1887–1951. WINCHELL MCK. CRAIG 117

Familial Haemangiomata of the Cerebellum. Report of Three Cases in a Family of Four. HENRIK O. TONNING, RUPERT F. WARREN, and HOWARD J. BARRIE 124

Sensory Changes with Herniated Nucleus Pulposus. LOYAL DAVIS, JOHN MARTIN and STANTON L. GOLDSTEIN 133

14114

Chordoma: Experience with Thirteen Cases. James L. Poppen, and Arthur B. King 139
Nonobstructive Hydrocephalus. Treatment by Endoscopic Cauterization of the Choroid Plexus. Long Term Results. John E. Scarff 164
Vascular Lesions in Pituitary Adenomas. C. F. List, J. R. Williams, and G. W. Balyeat 177
Pterional Meningiomas "En Plaque." Francesco Castellano, Beniamino Guidetti, and Herbert Olivecrona 188
A New Operation for the Relief of Pain in Angina Pectoris. John T. Robson 197
The Possible Use of Neutron-Capturing Isotopes such as Boron^{10} in the Treatment of Neoplasms. 1. Intracranial Tumors. William H. Sweet, and Manucher Javid 200

Case Reports and Technical Notes:

Apoplexy in a Pituitary Chromophobe Adenoma Producing the Syndrome of Middle Cerebral Artery Thrombosis. Case Report. Max T. Schnitker, and Harley B. Lehnert 210
Neurogenic Sarcoma Treated by Surgery and Radiotherapy. Edward S. Murphy, William R. Lipscomb, and John S. Bouslog 214
Cyst of a Cerebral Hemisphere Treated by Intraventricular Drainage. Douglas Miller 219
Case Report of an Adamantinoma Present at Birth. C. G. Subramani Iyer 221
Lumbar Disc Protrusion. A Useful Sign. Donald McEachern 229
A Self-Retaining Spinal Dura Retractor. Ralph B. Cloward 230

Notices 233

MAY 1952. No. 3

Cerebral Angiography in Children. An Anatomoclinical Evaluation. Jorge A. Picaza 235
Extradural Hematomas of the Posterior Fossa. Lloyd J. Lemmen, and Richard C. Schneider 245
A Comparison of Polyethylene and Tantalum for Cranioplasty. A Preliminary Report. Walter S. Lockhart, Jr., Gordon van den Noort, Warren H. Kimsey, and Robert A. Groff 254
Clinical Complications of Cerebral Angiography. Kenneth H. Abbott, James R. Gay, and Robert J. Goodall 258
Water Exchange of Central Nervous System and Cerebrospinal Fluid. Edgar A. Bering, Jr. 275
Decompression of the Trigeminal Root and the Posterior Part of the Ganglion as Treatment in Trigeminal Neuralgia. Preliminary Communication. Palle Taarnhøj 288

Extradural Cerebellar Hematoma. Report of Three Cases with Review of the Literature. A. J. Beller, and E. Peyser 291
Antony Chipault. 1866–1920. D. Petit-Dutaillis 299

Case Reports:

Sciatica Caused by Tumoral Calcinosis. A Case Report. Paul A. Riemenschneider, and Arthur Ecker 304
Torulosis of the Brain. A Case Report. Frank Padberg, and John Martin 307
Multiple Spinal Cord Meningiomas. Robert W. Rand 310

Notices 315

JULY 1952. No. 4

The Cerebellar Angioreticulomas. H. Olivecrona 317
Neurophysiological Studies on Cerebral Concussion. R. B. Aird, L. S. Strait, D. Zealear, and M. Hrenoff 331
Localized Encephalitis, Brain Abscess and Subdural Empyema. 1945–1950. E. H. Botterell, and C. G. Drake 348
Trigeminal Neuralgia. A Review of Six Hundred and Eighty-Nine Cases with a Follow-up Study on Sixty-Five Per Cent of the Group. Max M. Peet, and Richard C. Schneider 367
Effects of Intracarotid Administration of Nitrogen Mustard on Normal Brain and Brain Tumors. J. D. French, P. M. West, F. K. von Amerongen, and H. W. Magoun 378
An Evaluation of Palliative Surgical Procedures in Trigeminal Neuralgia. Everett G. Grantham, and Ludwig H. Segerberg 390

Case Reports and Technical Notes:

An Unusual Case of Unilateral Eighth Nerve Tumor. Vernon H. Mark, and William H. Sweet 395
Benign Arachnoid Cysts of the Posterior Fossa. William V. Trowbridge, and John D. French 398
Colloid Cyst of the Fourth Ventricle. Report of a Case of Two Colloid Cysts of the Fourth Ventricle. Dwight Parkinson, and A. E. Childe 404
Gliomatosis Cerebri. N. Malamud, B. L. Wise, and O. W. Jones, Jr. 409
Bed Attachment for Improved Head Traction. Charles F. Clayton 417

Notices 420

SEPTEMBER 1952. No. 5

Tumors of the Gasserian Ganglion. Tumor of the Left Gasserian Ganglion Associated with Enlargement of the Mandibular Nerve. A Review of the Literature and Case Report. Henry M. Cuneo and Carl W. Rand 423

Localization of Intracranial Lesions by Radioactive Isotopes. William T. Peyton, George E. Moore, Lyle A. French, and Shelley N. Chou 432
Subdural Hematoma Associated with Bleeding Intracranial Aneurysm. Robert C. Bassett and Lloyd J. Lemmen 443
Paragasserian Tumours. A. Ver Brugghen 451
Electrical Excitability of the Human Motor Cortex. I. The Parameters of the Electrical Stimulus. Murray Glusman, Joseph Ransohoff, J. Lawrence Pool, Harry Grundfest, and F. A. Mettler 461
Tangential Wounds of Scalp and Skull. Philip R. Dodge, and Arnold M. Meirowsky 472
Cerebellar Hemangioma (Hemangioblastoma). A Clinicopathological Review of 40 Cases. Maurice L. Silver, and Gordon Hennigar 484
Traumatic Internal Carotid Artery Thrombosis Secondary to Nonpenetrating Injuries to the Neck. A Problem in the Differential Diagnosis of Craniocerebral Trauma. Richard C. Schneider, and Lloyd J. Lemmen 495
Phantom Limb in Paraplegic Patients. Report of Two Cases and an Analysis of Its Mechanism. Albert W. Cook, and William H. Druckemiller 508
The Ocular Complications of Carotid Angiography. The Ocular Signs of Thrombosis of the Internal Carotid Artery. Frank B. Walsh, and George W. Smith 517
Our Training Programs and the Future of Neurological Surgery. Paul C. Bucy 538

Case Reports and Technical Notes:

Aneurysm of Anomalous Ophthalmic Artery Presenting in the Sphenoid Sinus and Simulating an Aneurysm of the Internal Carotid Artery on Routine Arteriography. Gordon J. Kinley, and David S. Leighninger 544
Transient Loss of Vision Following Cerebral Arteriography. Frank J. Otenasek, and James Markham 547
Double-Jointed Tantalum-Clip-Applying Forceps. Albert S. Crawford 551

Notices 553

NOVEMBER 1952. No. 6

Intracranial Tuberculomas. Experience with Ten Consecutive Cases. Antonio González-Revilla 555
Hypertrophic Spinal Pachymeningitis with Special Reference to Appropriate Surgical Treatment. Paul C. Bucy, and L. Willard Freeman 564
Orbitofrontal Lobotomy with Reference to Effects on 55 Psychotic Patients. John R. Green, R. E. H. Duisberg, and W. B. McGrath 579

The Electroencephalogram in Subdural Hematoma. LEWIS L. LEVY, LUDWIG H. SEGERBERG, RICHARD P. SCHMIDT, RICHARD C. TURRELL, and EPHRAIM ROSEMAN 588
Autonomic Pathways in the Spinal Cord. DONALD A. JOHNSON, GRACE M. ROTH, and WINCHELL McK. CRAIG 599
The Use of Refrigerated Autogenous Bone Flaps for Cranioplasty. GUY L. ODOM, BARNES WOODHALL, and FRANK R. WRENN, JR. 606
On the Anatomy of Anterolateral Cordotomy. EDGAR A. KAHN, and ROBERT W. RAND 611
Schistosomiasis of the Brain. FRANCIS A. CARMICHAEL, JR., and HOWARD S. COWLEY 620
Is there Room for a Neurologist in a Neurosurgical World? JOSEPH C. YASKIN 635

CASE REPORTS:

Chronic Subdural Hematoma in an Adult Producing Marked Erosion and Perforation of the Overlying Dura and Skull. Report of Case with Operation and Recovery. J. M. MEREDITH, and GEORGE R. GISH, JR. 639
Disseminated Oligodendroglioma. WILLIAM V. TROWBRIDGE, and JOHN D. FRENCH 643
Paraplegia from Ruptured Lumbar Discs in Achondroplastic Dwarfs. FREDERIC SCHREIBER, and HERBERT ROSENTHAL 648

NOTICES 652
Index to Volume IX 653

FAT EMBOLISM

A PROBLEM IN THE DIFFERENTIAL DIAGNOSIS OF CRANIOCEREBRAL TRAUMA

RICHARD C. SCHNEIDER, M.D.

Section of Neurosurgery, Department of Surgery, University Hospital, Ann Arbor, Michigan

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IN SPITE of the frequency with which fat embolism involves the central nervous system there have been few reports written by neurosurgeons and neurologists on this topic. A consideration of fat embolism is important in the differential diagnosis in patients who have received extensive lacerations or long bone fractures concomitantly with head injuries. Within a period of 6 months 3 patients with lesions of this type have passed through the Neurosurgical Service at University Hospital. In addition to fractures of various long bones the tentative diagnoses in these cases at the time of admission were extradural hemorrhage, subdural clot, and midbrain injury, respectively. Following is a brief presentation of these 3 cases.

CASE REPORTS

Case 1. M.B., a white female aged 20, was admitted to a local hospital at 3:00 A.M. on July 30, 1950 after being injured in an automobile accident. She suffered a simple fracture of the right femur and the left tibia, and multiple lacerations about the head and left groin. At admission the patient was conscious and her neurological status was negative. The fractured extremities were placed in casts. About noon she became progressively more stuporous and at 5:00 P.M. her physician noted a dilated pupil and bilateral pyramidal tract signs and transferred her to University Hospital.

By 9:30 P.M. a definite paresis of the left arm had developed and there were focal seizures of the left side of the face. B.P. 140/100, pulse rate 106, and respirations 22. A diagnosis of probable right temporoparietal extradural hematoma was made.

Operation, July 30, 1950. Multiple burr holes were made bilaterally, but no epidural or subdural hematoma was found. There was some evidence of contusion at both frontal trephine holes and the brain pulsated freely with no tendency to extrude.

Course. Her condition remained unchanged until 48 hours postoperatively when it was observed that respirations had become more labored. The pupils were still equal. Petechial hemorrhages appeared on the skin of the neck, trunk and upper extremities (Fig. 1) and the diagnosis of fat embolism was suggested. Fat globules in the urine confirmed the diagnosis.

On Aug. 4, 1950 the ophthalmological consultant found ecchymosis of the left eyelid with occasional petechial conjunctival hemorrhages. The right fundus displayed a slight cloudiness of the media due to fat droplets. The disc margins were distinct. Along the superior and inferior temporal vessels there were large cotton-wool exudates, and about the macula there was a gray cloudiness of edema. An oc-

casional superficial hemorrhage was present. The pattern was similar in the left fundus except there were more superficial hemorrhages and no large exudates.

On August 9, after an attempt was made to reduce the fracture in the right leg a marked spasticity developed in all extremities, but a week later the patient appeared definitely improved and responded to verbal stimuli.

On August 17 her temperature rose suddenly to 102°F., pulse to 160, and B.P. to 160/90. There was onset of clonic twitching and jerking of extremities with intermittent periods of complete extension and marked opisthotonos. She gradually

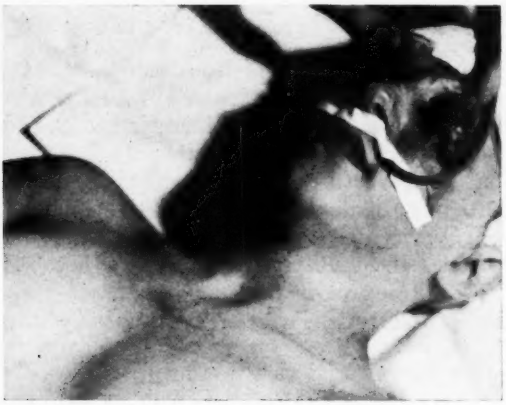

FIG. 1. *Case 1.* The periorbital ecchymosis associated with the head injury is demonstrated. Unfortunately the petechial hemorrhages of the skin of the neck and upper chest are not readily visualized.

improved, passing through a stage of decerebrate rigidity during which she moaned and groaned almost constantly. Because of the severe extensor spasms of her lower extremities resulting from the lesions of the central nervous system, it was necessary to permit 2 inches of shortening of the right femur.

The patient was discharged on October 15 in a bilateral hip spica. Her mental status had improved markedly, but there was still emotional lability.

On April 10, 1951 a follow-up examination revealed that the patient was mentally sound and alert. The fundi were normal. A mild Horner's syndrome was observed on the left. Tonus was normal in all extremities, but a minimal left hemiparesis was elicited with bilateral pyramidal tract signs. Her general condition was excellent and there was daily improvement in her neurological status.

Comment. The chronological appearance of symptoms should be reviewed. The onset of mental confusion and lethargy occurred about 12 hours after the accident, a short time after a cast had been applied to the left leg, suggesting the liberation of a shower of emboli. Fat globules were found in the urine 60 hours after the accident. The petechial hemorrhages on the skin of the neck, trunk, and upper extremities and the abnormal fundi were observed on the 3rd and 4th days after injury, respectively. Within 9 days after her admission the patient had improved markedly but suddenly there was temperature elevation with onset of tonic seizures of the extremities indicating the release of another deluge of fatty emboli to the brain stem

or the vicinity of the basal ganglia. Judging from her past improvement, recovery from neurological sequelae should be almost complete.

In a patient who has sustained a head injury 12 hours previously the development of a dilated right pupil with bilateral extensor plantar reflexes suggests the formation of a tentorial pressure cone due to a rapidly expanding right temporoparietal extradural hematoma. If such a case is observed until there are changes in vital signs the patient is apt to succumb before operation can be performed. Therefore, trephination was indicated even though a diagnosis of fat embolism could have been made, for extradural hematoma and fat embolism might coexist.

Case 2. J.F., a white female aged 24, was admitted to a local hospital early on the morning of Feb. 25, 1951 after sustaining injuries in a traffic accident. She was unconscious, had bleeding from the nose, and vomited old blood on several occasions. On February 26 she was semiconscious but did not respond sufficiently to painful stimuli to answer questions. A portable x-ray indicated that there was a fracture of the anatomical neck of the left humerus. On February 28 she was quite alert and her left arm was placed in traction. By the following day she was less responsive and there was nuchal rigidity; that evening there was elevation of temperature, she became more restless, and incontinent of bladder and bowel, and a motor aphasia developed. A lumbar puncture was performed by her physician who observed that there was a "highly colored" spinal fluid under increased pressure (not measured by manometer) and a normal cell count. She was admitted to the University Hospital on March 4, 1951.

Examination. Temperature 102°F., pulse 80, respirations 20, and B.P. 108/70. The patient understood questions, at least partially, and could be readily aroused. The left arm was bound firmly to the chest above the elbow. There were numerous contusions and abrasions of the legs, face and head including a bilateral Battle's sign. Periorbital extravasation was present on the left with subconjunctival hemorrhage. Marked nuchal rigidity was found on attempting any movement of the head and neck. The pupils reacted equally to light, and the fundi were normal, but there was definite dissociation of eye movements. Accurate evaluation of sensation was impossible. Weakness and hypotonia were found in both lower extremities. The reflexes were slightly more hyperactive on the right than the left, and bilateral pyramidal tract signs were elicited. Skull x-rays revealed no fracture.

A tentative diagnosis of fat embolism was made, and on two occasions fat globules were demonstrated in the urine.

Course. By March 13 the dissociation of eye movements had vanished, and the patient began to use isolated words and became mentally clearer. A few days later her arm was placed in a hanging cast, and she was permitted to be up and about. At the time of discharge on April 1, 1951 she acted in a euphoric and flippant manner, but her neurological findings were otherwise negative.

Comment. The history in this case suggested a subdural hematoma, and the neurological findings of aphasia and bilateral pyramidal tract signs indicated that such a clot might lie over the left hemisphere. However, the fact that the pupils were equal, the patient was moderately alert, and dissociation of eye movements had been observed implied that the lesion was a diffuse rather than a localized one. Because of the fracture of the left

humerus and our experience with Case 1 the urine was tested for fat droplets and the diagnosis of fat embolism was confirmed. The patient was spared unnecessary trephination. There was no sputum available for testing, the eyegrounds were negative, and there were no petechiae on the skin or in the conjunctival sacs.

Case 3. W.W., a colored male aged 29, was admitted to the University Hospital at 7:30 P.M. on Aug. 3, 1950, 1½ hours after being severely injured in a highway accident.

Examination. He was unconscious and did not react to pin prick stimulus, but did resist any movement of the injured lower extremities. B.P. 140/65, pulse 140,

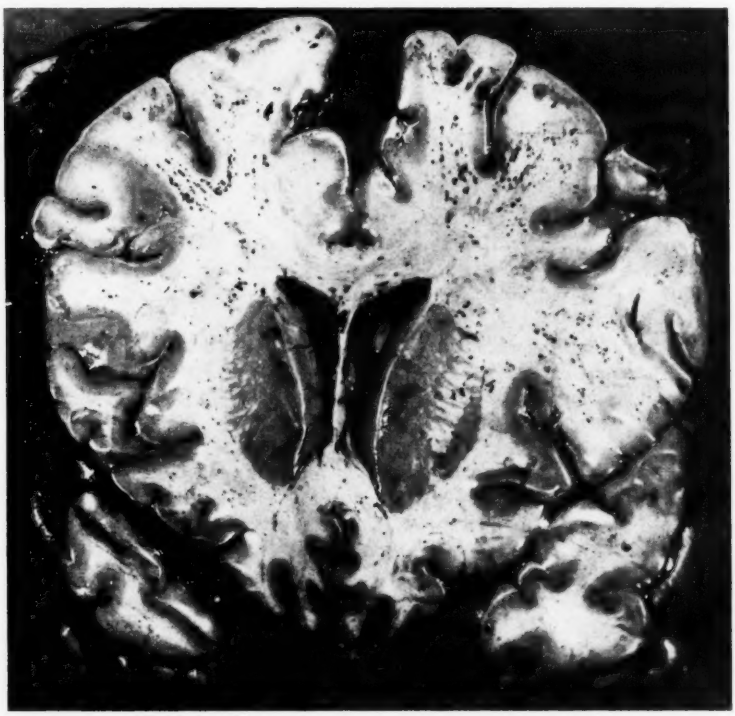

FIG. 2. *Case 3.* Specimen showing the multiple petechial hemorrhages scattered throughout the gray and white matter.

and respiration 28. There were two deep lacerations of the scalp in the left parietal and occipital regions. Both legs had compound fractures in their middle third. The breath sounds were diminished over the right chest but normal on the left with moist gurgling rales. The pupils were equal and reacted to light and the fundi were normal. The reflexes were equal and there were no pyramidal tract signs in the upper or lower extremities.

Course. On the following day there were tonic extensor contractions of all four extremities whenever the patient was stimulated. The respiratory rate increased to

42 per minute and the temperature rose to 104°F. Large quantities of sputum were aspirated, but none was tested for fat. The patient received penicillin intramuscularly, oxygen by nasal catheter, and intravenous fluids. Two urine examinations were negative for fat globules, one of them 24 hours before his death. A clinical diagnosis was made of severe brain stem damage, bronchopneumonia, and compound fractures of both lower extremities. At no time was there any sign of increased intracranial pressure as evidenced by rise in blood pressure or drop in pulse rate. The patient died on Aug. 8, 1950 at 6:00 A.M.

Autopsy. The brain was edematous, and in cross sections many tiny petechial hemorrhages were seen in both the white and gray matter (Fig. 2). Microscopically there were characteristic hemorrhagic infarcts or ring hemorrhages[29,36,42] consisting of a thrombosed arteriole with a surrounding zone of necrosis and at the periphery a large ring of red blood cells. On fat stain the globules could be demonstrated in the capillaries and perivascularly there were large collections of erythrocytes. Another type of cerebral lesion was the circumscribed oval-shaped pale areas of necrosis, an anemic infarct (Fig. 3). In these there was complete destruction of cells and fibers with a thinned out or rarefied area. In the center an occluded vessel was occasionally found. There were no petechial hemorrhages in the midbrain, but a number were clumped near the basal ganglia supratentorially. Unfortunately, the choroid plexi were not examined, for Russell[26] has studied 2 fatal cases of fat embolism in which the plexi showed a conspicuous blockage of the capillaries and arterioles with fat.

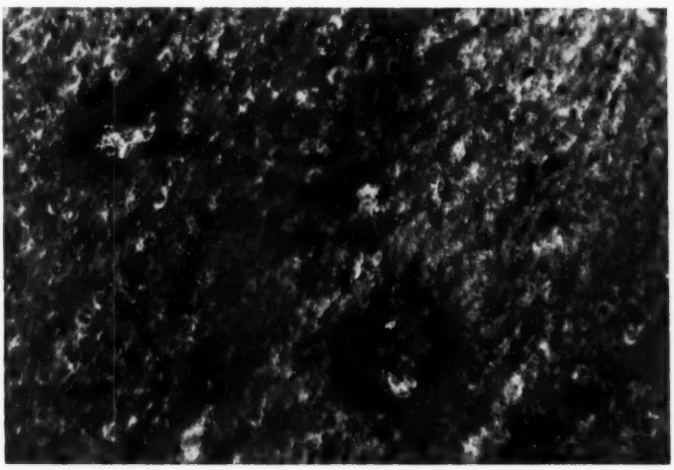

FIG. 3. *Case 3.* Photomicrograph of section of the brain stained for fat, showing a cerebral vessel with perivascular collection of fat globules and red blood cells. Note the light area of destruction around the periphery indicating an anemic infarct.

Grossly the lungs were heavy and hemorrhagic, and a puriform exudate could be expressed from the cut surface. On microscopic examination of a section stained for fat vast numbers of fat globules were found in the alveoli, alveolar capillaries and arterioles. A massive inflammatory exudate was present in all lobes, indicating a diffuse lobular pneumonia.

Specially stained sections of the kidneys revealed an abundance of fatty emboli

within the glomerular capillaries. Scattered fat globules could be found in the tubules.

Comment. Clinically this patient had a neurological pattern suggesting a midbrain injury. During his course there was no significant progression in findings or change in vital signs that might indicate a surgical lesion. The tonic seizures of the upper and lower extremities were similar to those seen in cases of midbrain damage although the same pattern may be seen in cases where petechial hemorrhages have occurred bilaterally in the vicinity of the basal ganglia. Postmortem examination subsequently proved the latter type of involvement was probably responsible for the seizures.

It is significant that fat was sought in the urine in vain on two occasions, one of them 24 hours before death, and yet microscopic postmortem examination of the kidneys revealed an abundance of fat in the glomerular capillaries. Unfortunately the sputum had not been checked for fat globules. The fundi had been observed on several occasions but no abnormalities were found, and there were no petechial hemorrhages on the skin.

In this case there was no difference in the treatment of the lesion due to trauma than for the state of diffuse fat embolism. The latter diagnosis was suspected but could not be demonstrated until postmortem examination.

FAT EMBOLISM

The literature on fat embolism has been completely reviewed in the past by several authors: Scriba,[31] Warthin,[39] Groskloss,[12] Gröndahl,[11] and Scuderi,[32] so that only a few historical facts will be noted here in a discussion of the topic.

According to Flournoy,[8] Lower (1669) first attempted experimentally to produce fat embolism by injecting milk intravenously in dogs. In 1860 Cohn[5] reported fat emboli in the cerebral capillaries of man, but believed that they were merely metabolic products of the degenerating cerebral vessel wall. Scriba[31] (1880) regarded embolic phenomena in the spinal cord and brain as one of the primary factors in causing death.

Incidence. The incidence of fat embolism cannot be determined accurately.[16] Out of 59 patients with long bone fractures, Vance[36] found that at autopsy 20 per cent had severe fat embolism, which could have been the cause of death, whereas 75 per cent of the group exhibited some minor degree of this condition. Compare these civilian injuries to a series of 1000 consecutive battle casualties reported by Wilson and Salisbury.[41] There were 119 cases of fractured long bones, in 8 of which fat embolism occurred; 6 of the patients died of the lesion. Ryerson[27] and Utgenannt[35] have reported fat embolism in children as young as 8 months and 8 years of age, respectively. However, most of the reported cases of the entity occurred in the third to fifth decade. The reason given is that in adult tissues there is a greater proportion of olein than in childhood. This substance is more fluid at body temperature than either palmitin and stearin. It is, therefore, more readily mobilized and thrown into the circulation as emboli.

Source. According to Winkelman[42] the commonest sources of fat embolus are the marrow of the long bones, subcutaneous tissues, lipaemic conditions associated with diabetes, various parenchymatous states, etc. Gauss[9] has stated that there are three essentials before fat embolism can occur: "1. An accumulation of fluid fat freed from its combined state by trauma. 2. Force must tear adjoining vessels to permit entrance of the fat into the circulation. 3. The accumulation of the fat must be under a pressure greater than venous pressure so that it can be driven into the vessel." The source of the trauma may be a fracture of the long bones, blast injuries, severe bruises, and soft tissue injuries. However, de Gutiérrez-Mahoney[13] has been able to demonstrate experimentally shattering of the myelin sheaths in the cerebral white matter of dogs by blows upon the cranium, and it is his conception that the fat that occludes the cerebral vessels is derived locally from this disintegrated myelin. There is not only an interruption of many cortical fibers, but there is a fatty occlusion of the cerebral vessels as well, with resulting hypoxia to cells that have already been damaged by concussion. These experimental lesions were identical with those of patients who had died of cerebral fat embolism. In Warren's[38] series of 100 cases of fat embolism in which autopsy was done, there was a history of trauma to the head in one-third, but it was felt that there was no correlation between the injury and the fat embolism of the brain.

Once the fat globules have reached the venous system, whatever may be the mechanism, they are carried to the pulmonary capillaries, where a certain number will occlude the vessels, and another portion will pass through and enter the left side of the heart to be pumped into the arterial circulation. This is the generally accepted view. Vance[36] believed that fat could enter the systemic circulation through the pulmonary capillaries or through a patent foramen ovale in the cardiac septum. A third possibility is that fat may be transported directly through the vertebral veins to the brain, the pathway described by Batson[1] for metastases from the breast or pelvis to the cerebrum. This course of distribution would by-pass the lung and would be contrary to Warren's belief that cerebral fat embolism cannot occur without some degree of pulmonary involvement.

Diagnosis. By far the most important single factor in the diagnosis of fat embolism is an awareness that it can, and often does, exist in traumatic cases of mild as well as severe type. The "symptom-free interval," a period during which the patient's general condition is good except for the result of his initial injury, has been emphasized by Robb-Smith[24] as a characteristic feature. Winkelman[42] has estimated that there is a 3- to 6-day average interval before the appearance of symptoms, but stated that the shortest free interval reported was 30 minutes and the longest, 9 days.

Excluding these features we find that little has been added to the criteria in the diagnosis of fatty embolism since the publication of Warthin's classical article. These factors will be listed and enlarged upon:

"1. *Injury to the bone marrow or adipose tissue.*" It should be emphasized that the severity of fat embolism is not directly proportional to the degree of

tissue injury. Fatal cases have been reported following relatively slight episodes of trauma.

"2. *A cardiac, pulmonary or cerebral complex of these combined (restlessness, stupor, coma, dyspnea, cough).*" The cardiac symptoms usually consist of an increase in pulse rate with a fall in blood pressure and a rise in venous pressure. However, pulmonary and cerebral symptoms usually dominate the picture. There may be a sudden onset of increased respiratory rate, cough, stertorous breathing, cyanosis, and rales in the chest suggesting a marked bronchopneumonia. The cerebral symptoms may consist of increased restlessness, loss of sphincter control, generalized disorientation, and gradually deepening coma. Tonic and clonic seizures may occur. Aphasia and hemiplegia may be present, but it should be stressed here that evidences of a diffuse involvement of the central nervous system should be sought suggesting scattered multiple petechial hemorrhages secondary to fat emboli. Headache, nausea, vomiting, papilledema, and other signs and symptoms of increased intracranial pressure are usually absent.

"3. *Free fat droplets in the sputum: Fat containing alveolar cells in the sputum.*" Warthin (1913) was the first to call attention to this as a valuable laboratory test. Scott and Kemp[30] have observed that we should not expect a significant amount of fat in the sputum until at least 36 hours have elapsed after the onset of the pulmonary symptoms. Most writers agree that the finding of fat in the sputum is of diagnostic value, but Lehman and McNattin[20] feel that it is not pathognomonic, and that fat can occur in the alveoli of the lung without fat embolism. Chest x-rays may show considerable diminution of translucency of the lung fields with a diffuse mottling of acute pulmonary edema. Sufficient fat may be present in the lungs to cause respiratory embarrassment without any significant x-ray changes.[30]

"4. *Free fat droplets in the urine.*" Scriba[31] (1880) reported finding fat in the urine in 80 per cent of his patients with fat embolism 2 to 6 days after sustaining a fracture or undergoing a bone operation, and stated that it may disappear only to reappear again in 8 or 13 days. The urine must be obtained by catheter to insure that the bladder has been completely drained, for fat will tend to float on the surface and may remain behind with any residual urine. An oily lubricant, of course, must not be used upon inserting the catheter.

One obvious point is frequently overlooked, namely, that in examining the urine or sputum for fat a control test should be performed on a specimen of distilled water to check the stain. Recently upon testing the urine of a patient suffering from fat embolism and a control tube of distilled water one of our alert interns found that globules of fat were present in both. The bottle of Sudan III had been contaminated by an oily substance.

"5. *Examination of the eye grounds for evidence of fat in the circulating blood.*" The presence of fat globules in the retinal vessels of a patient who had fat embolism was reported by Oppenheimer[22] (1929). However, not much emphasis was placed upon the fundus until Urbanek[34] described his

retinal findings in 4 of 8 cases of fat embolism. He pointed out that because of the customary absence of visual symptoms there were infrequent examinations of the fundi and many lesions were missed. The fundi primarily displayed small hemorrhages and white exudates simulating a diabetic retinitis, but he noted particularly that the pattern was a dynamic one so that with the disappearance of one group of lesions there might be the occurrence of an entirely new crop of hemorrhages and exudates. The fat globules themselves are rarely seen in retinal vessels. Evans[7] reported a case in which the fundus changes were found on the third day after injury. In addition to the subhyaloid hemorrhages and the exudates, a diffuse edema of the retinae was discovered. Scattered crescentic zones of pallor were also visualized. Within a week the edema began to subside and the hemorrhages began to undergo absorption. Newman,[21] in reporting the clinical findings on 7 patients with fat embolism, found the above-described lesions in 4 of them. Walsh[37] describes 1 case thoroughly which he had observed.

"6. *Examination of venous blood for fat droplets.*" Scuderi[32] felt that darkfield examination of the blood for fat globules would be most helpful. However, this procedure has been of little value in making the diagnosis of fat embolism. It should be mentioned that most writers are of the opinion that the size of the fat globules is of much greater importance than the total amount of fat in the blood.[38,41,42]

"7. *Increase of temperature, rather than a lowered temperature as reported by Scriba and as quoted in the textbooks.*" A rapid rise of temperature without evidences of pneumonia suggests that the brain has been involved in an embolic process.[14,38,42]

"8. *Examination of the skin for petechial hemorrhages.*" These are prone to occur over the chest, base of neck, upper extremities, and the conjunctival sacs. Their number bears no relationship to the prognosis of the case.[21] They have been reported by Benestad,[2] Busch,[3] Corlette,[6] Killian,[17] and others. On the average the petechiae may occur 3 days after injury, but Warthin has reported their occurrence as early as 12 hours after an episode of trauma. Wilson and Salisbury[41] have stressed that while these petechiae are due to definite emboli which tend to slow down the general circulation, they are by no means a constant finding.

Treatment. Many forms of treatment have been prescribed, but there is still no single effective method of dealing with the problem. Prophylaxis in the form of adequate splinting during transportation and careful manipulation of fractures have been suggested by Robb-Smith[24] and others. Avoidance of tight casts or bandages and the aspiration of hematomas prevent a building-up of local pressure at sites of injury, and have been advocated by Harris, *et al.*[15] Schanz[28] used intravenous physiological saline to flush out the cerebral capillaries, but this is not without danger if there is cardiac failure, pulmonary congestion, or cerebral edema. Injection of a 2 per cent solution of sodium carbonate intravenously with the hope that it might combine with fat to form a soluble soap was suggested by Warthin in 1913, and was

again revived by Wegelin[40] in 1923. Klapp[18] ligated the femoral vein and Newman[21] tied off the profunda vein in the hope of preventing the propagation of more fat emboli into the circulation. Rappert[23] suggested the use of sodium desoxycholate intravenously to emulsify fat and cut down on its viscosity. Robb-Smith[25] has used this experimentally and also clinically in 1 case, but his results tend to indicate that this method is definitely harmful.

It is apparent that there is no effective specific therapy at the present time. Active use of supportive measures is of considerable value. Adequate intratracheal suctioning to remove pulmonary secretions and permit the access of oxygen to the alveoli should be carried out vigorously in order to prevent further cardiac and cerebral anoxia. Venesection perhaps should be performed in cases of acute cardiac failure, but adequate digitalization and the use of hypertonic solutions may restore the circulatory balance.

Another problem is the adequate control of convulsive seizures of either the tonic or clonic variety. The early employment of sufficient quantities of barbiturates parenterally at the first evidence of such episodes will prevent frequent seizures or status epilepticus with its associated frothing at the mouth, aspiration of secretions and danger of hypostatic pneumonia. With these controlled there will be less tendency for fresh emboli to be thrown into the circulation by friction at a fracture site during a convulsion. The prevention of cerebral hypoxia should be the aim of all therapy in order to diminish the likelihood of irreversible changes in the central nervous system.

Most of the characteristic pathological changes occurring in fat embolism involving the brain, lungs, and kidneys have been briefly described in Case 3.

Differential Diagnosis. Thus far the discussion has dealt primarily with fat embolism alone, but when head injury occurs simultaneously the differential diagnosis becomes much more difficult. Reference may again be made to Warthin's publication to obtain one of the first discussions of the problem: "The occurrence of a free interval in many cases of fatty embolism will distinguish them from shock, commotio cerebri and contusio cerebri. In the case of meningeal hemorrhages and compressio cerebri the differential diagnosis is at times very difficult."

In the series of 13 cases of fat embolism which he described in some detail there were 5 patients who had sustained head injuries as well as fractured long bones. Four of these patients were unconscious or semi-conscious on admission to the hospital. Four died unoperated upon and 2 of these had extradural hemorrhages; the fifth was trephined and no lesion was found.

Harris, *et al.*,[15] Krönlein and Wiesmann,[19] and Tobler[33] reported cases of fat embolism in which a mistaken diagnosis of epidural hematoma was made, and the patient operated upon. Winkelman[42] states: "The condition which most nearly simulates fat embolism in the early stage is epidural hemorrhage, but in the latter pulmonary signs and symptoms are usually absent and there is characteristically hemiparesis which gives the clue to the true nature of the condition." In commenting upon the differentiation from

intracranial hemorrhage, Godlee and Williams[10] observed that in fat embolism there is a superficial resemblance to compression of the brain without pulse compression.

The criteria for operation in head injuries are usually well defined. The gradual loss of consciousness after head trauma is one of the cardinal ones. The progression of neurological signs, particularly the development of a tentorial pressure cone, demands early operation. Evidences of increased intracranial pressure as demonstrated by an elevated blood pressure and bradycardia require prompt surgical treatment.

Because of the course in Case 1 and Case 2, we may have to inspect our criteria for trephination in cases of head trauma. Usually during the first 24 hours there are no clinical signs of fat embolism on which to rely other than the possibility of scattered neurological findings which might indicate a diffuse involvement of the central nervous system. This is the so-called "free interval" of fat embolism and coincides with the "lucid interval" of extradural hemorrhage. The most characteristic finding in epidural hematoma is the development of signs of a tentorial pressure cone. If this pattern is present, namely a dilated pupil and bilateral pyramidal tract signs, immediate trephination is essential if the patient is to survive. To await a hemiparesis as a clue to the lesion or procrastinate until there is a compression pulse spells disaster, and is probably one of the reasons why the mortality rate is so high in cases of extradural hematoma. There is no reason why fat embolism and epidural hemorrhage cannot coexist, as was observed in 2 of Warthin's cases. If there is any doubt, trephination should be carried out.

However, if an interval of 3, 4 or more days has elapsed from the time of injury, a fatty embolic lesion may be confused with subdural hematoma, as occurred in Case 2. By this time fat may be found in the urine or sputum, or, upon examination of the eyegrounds, conjunctival sacs, and the skin, petechial hemorrhages may be found and aid in the establishment of a diagnosis of fat embolism. The presence of pulmonary symptoms resembling bronchopneumonia or scattered cerebral signs tends to lend further support to this impression.

Jostling the patient about in order to procure skull x-rays is in most instances a procedure to be condemned, for this may only cause more trauma at the fracture site, and the patient is often too restless to obtain x-rays that are not clouded by movement. Occasionally a shifted calcified pineal gland might be demonstrated or a fracture line identified crossing the middle meningeal groove, but this is too infrequent to justify the attempt.

After carefully reviewing a considerable segment of the literature on the subject of fat embolism, we have found only 1 case report in which fat was found in the spinal fluid.[4] However, the question may well be raised as to how frequently it has been specifically sought. In practically all instances cerebrospinal fluid pressure was normal, and there was no abnormality in the routine chemical studies. However, there is no indication that lumbar

puncture will aid significantly in the diagnosis of either head injury or fat embolism, and the patient's resistance to spinal tap may cause further fat emboli to be given off at a fracture site.

In conclusion it may be said that one should be aware of the possibility of fat embolism in cases of head trauma with other multiple injuries. If there is any doubt that a surgical lesion does exist, a negative trephine hole does no harm, and it is far better to err in this direction.

Since 2 of our 3 patients with cerebral fat embolism recovered, we feel that the prognosis must be guarded, but need not necessarily be considered hopeless as has been reported in the past.

SUMMARY

The problem of the differential diagnosis of fat embolism in cases of craniocerebral trauma has been discussed with a presentation of 3 cases which simulated extradural hemorrhage, subdural clot, and midbrain injury, respectively. The signs, symptoms and laboratory studies for identifying fat embolism have been reviewed. The most important single point in the problem is an awareness that such a lesion exists. If there is any doubt about the coexistence of an intracranial clot and cerebral fat embolus trephination should be carried out.

ADDENDUM

Since this paper was forwarded for publication another case was seen on the neurosurgical service.

Case 4. R.S., a white male aged 26, was admitted to a local hospital shortly after being injured in a motorcycle accident at midnight on Sept. 9, 1951. He was unconscious for about 1 hour and had sustained compression fractures of D6 and D7 vertebrae, a transverse fracture of the right femur and an oblique break in the right metacarpal. Several unsuccessful attempts were made to reduce the fractured right femur by manipulation. On Sept. 12, 1951 he became semicomatose and was sent to University Hospital with a diagnosis of subdural hemorrhage.

Examination. Temperature 100°F., pulse 96, respirations 24, and B.P. 156/106. He was semicomatose but could be roused. The only other positive neurological finding was a slight left facial weakness. A solitary petechial hemorrhage was found in his left conjunctival sac. Fat globules were demonstrated in the urine. A lumbar puncture was performed cautiously, yielding xanthochromic CSF under normal pressure and containing fat particles. The B.P. rose to 190/120 but the pulse rate remained elevated at 104 per minute and the patient could be roused. A diagnosis of cerebral fat embolism was made, and the patient was carefully observed for concomitant subdural hematoma.

Course. On the following day he was very alert and his vital signs had returned to normal. The orthopedic consultant felt that the fractured right femur was not well splinted and that there was danger of movement at the fracture site with more emboli being cast off. The right lower extremity was therefore placed in balanced traction. On September 15 the patient was very alert but had headache, dizziness, and anisocoria, the left pupil being larger than the right. Petechiae were observed over the chest. By the following morning the pupils were again equal.

Comment. This patient may still have to be trephined for an associated hematoma, but all findings may be due to cerebral fat embolism. In Case 1 the patient had a slight elevation of her diastolic blood pressure but continued to have a rapid pulse rate. In Case 4 there was a marked elevation of both the systolic and diastolic pressures which again returned to normal. In both cases there must have been a direct involvement of the vasomotor center by embolism, for the rise in each instance was only transient and the pulse remained rapid. One must be careful to differentiate this from increased intracranial pressure with its bradycardia. It is not known whether there is any definite time interval after which it is safe to manipulate a fracture without danger of throwing off a shower of emboli. In Case 4 immobilization of the fracture site was considered important to prevent further fat emboli.

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A STUDY OF THE CAUSES OF FAILURE IN THE HERNIATED INTERVERTEBRAL DISC OPERATION

AN ANALYSIS OF SIXTY-SEVEN REOPERATED CASES*

JAMES GREENWOOD, JR., M.D., T. H. McGUIRE, M.D., AND FARISS KIMBELL, M.D.

Department of Surgery, Baylor University College of Medicine and Methodist Hospital, Houston, Texas

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WHILE the percentage of good results following lumbar disc operations is high in the hands of capable neurosurgeons, all must admit a few failures and recurrences. Of 632 patients operated upon by us for herniated disc, 58 have had reoperations. Nine additional patients operated upon received their first surgery elsewhere (total 67). Although this group may seem large, it includes 10 patients reopened while they were still in the hospital and 16 who had an entirely different location for a second herniation. Many were operated upon after several years of complete relief before recurrence of pain necessitated a second procedure. Thus only 32 cases can be assigned to failure of surgery, a percentage of 5.0. An analysis has been carried out in detail with particular reference to the pathology found at the time of the second operation, procedures done to relieve the patient, and the results obtained. We have avoided reference to psychoneurosis as much as possible while fully realizing its importance. It is particularly prominent in compensation cases where the subconscious desire for a large settlement precludes the possibility of cure until this end is attained. Malingering does not have to be considered since such individuals seldom submit to a single operation, much less a second.

A search of the literature disclosed only one contribution (that of Campbell and Whitfield[2]) dealing with the reasons for failure of the disc operation. These authors emphasized psychological and compensation factors as causes for failure. The results of disc operations at L4 were not as good as at L5. Age, duration of symptoms, neurological and orthopedic changes did not seem to be significant. Bradford and Spurling[1] in their excellent monograph urge complete removal of the nucleus to avoid recurrence. Echols[3] has reported an instance of a second disc herniation at a new location, requiring another surgical procedure. While the presence of a bilateral herniation from one disc is rare, and double disc involvement less common, such a possibility must be considered when there is definite myelographic or clinical evidence of multiple protrusion. Of 16 patients reoperated upon, 6 possibly had a second disc at the time of the original operation which might have

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been removed if we had not been content to stop with the removal of one herniation.

The results of reoperation have not only been gratifying, but the knowledge gained has enabled us to improve an already acceptable percentage of good postoperative results in cases of lumbar herniated discs. For simplicity in tabulating results, "good" refers to patients who are able to resume their former occupation in comfort. Results classed as "not good" include improved or unimproved patients who must carry on at least with significantly reduced efficiency. Competent orthopedic consultation was freely used and followed in most cases, since it was felt that only through the combined efforts of both specialties could the greatest progress be made.

PATHOLOGY FOUND AT SECOND OPERATION

Of the 67 patients who were subjected to a second operation, 16 had a new herniation either at the side opposite from the previous herniation or at a new level on the same side; 17 had recurrence of cartilage at the same site as the previous rupture; 4 herniations were missed completely at the first

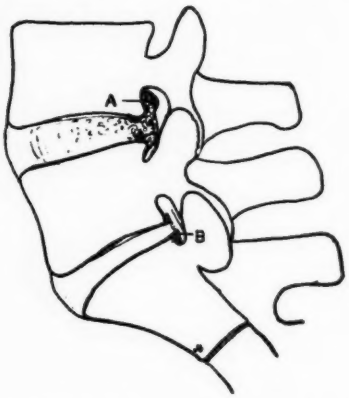

FIG. 1. (A) Evaginated cartilage which if not removed with herniation over interspace may still continue to compress nerve root. (B) Hyperostosis which may compress nerve root against overhanging facet.

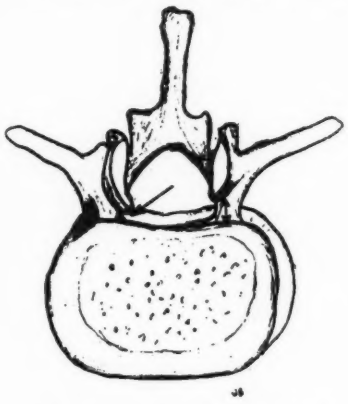

FIG. 2. Acute lateral angle (left side) formed by pedicle, facet, and body of vertebra. Adherent nerve root will be traumatized by motion at the interspace (root leaves spinal canal at interspace below). Normal clearance is shown on the right.

operation for one reason or another. Dense adhesions around the nerve root with or without bony encroachment (Figs. 1 and 2) were most common of all and occurred in 24 cases. X-rays were studied from the standpoint of hypertrophic changes, increase or loss of lordosis, and congenital anomalies, so that a comparison of the frequency of occurrence of these factors with that in an average group of operated disc cases might be made.

Particular notice was taken of the fact that at times the pathology was not limited to finding of a herniation at the interspace. In addition there was

often a loose piece of cartilage which had migrated laterally, cephalad, or caudad (Fig. 3). One case was seen in which herniation at the level of the 3rd lumbar disc had migrated down to compress the lumbar 5th root arising at the 4th interspace. While such migration accounted for only 4 reoperations, the knowledge gained prevented such oversight in other cases. A most interesting cause of failure was concealment by the retractor of a piece of loose cartilage which it carried back with the adherent nerve root. In spite of removal of disc contents, this sequestrated mass would slip back to compress the nerve root as soon as the retractor was removed (Fig. 4).

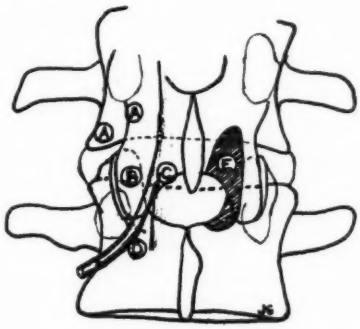

FIG. 3. (A, B, C, D) Locations from which loose pieces of migrated cartilage have been removed. (E) Bony exposure deemed necessary to insure that such migrations are not missed.

In some cases, even after the removal of a herniation, the nerve root was still firmly held between the evaginated cartilage edge or hyperostosis and the edge of the lamina above. Any motion at this interspace would tend to keep the nerve in an irritated, inflamed condition. In some cases there is an acute lateral angle between the facet and body of the vertebra (Fig. 2) which is sure to engage the nerve, and pressure will persist after surgery. The relief of symptoms following simple decompression has led us to make certain that no such narrow bony pathway is left unrelieved at the time of first operation. In many cases the opening is adequate and needs no attention except removal of the herniation.

Causes of failure and results of reoperation are summarized in Tables 1 to 7.

SUMMARY AND CONCLUSIONS

Sixty-seven cases of lumbar disc herniation in which reoperation was performed have been reviewed from the standpoint of pathology and re-

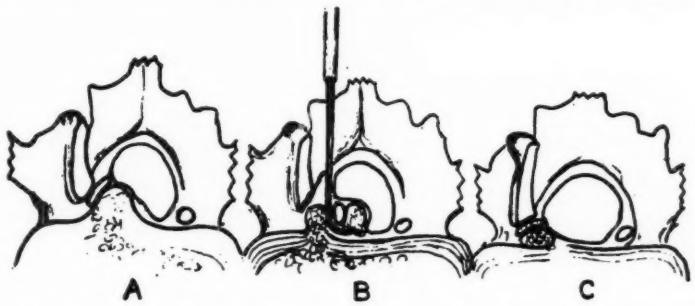

FIG. 4. Illustrates how cartilage adherent to nerve root is hidden by retraction, but returns to compress the nerve root. Gentle pressure above the nerve root will demonstrate that it is still compressed.

TABLE 1

Recurrent pathology and results

Pathology	Total	Good Results
New disc herniation	16	12
Recurrent disc	17	17
Adhesions, bony compression, or both	24	13
Nerve root section	13	8
Unilateral chordotomy	2	2
Simple decompression	9	3

TABLE 2

Reoperated cases—no disc found, or migrated cartilage missed at first operation

Pathology	Total	Results	
		Good	Not Good
No disc found first operation	9	6	3
Herniation removed second operation	4	4	0
Granulomatous infection of disc	1	1	0
Fused at second operation	2	1	1
Root sectioned	1	0	1
Postoperative hematoma	1	0	1
Migrated cartilage	4	4	0

TABLE 3

X-ray findings correlated with results of second operation

	Total	Results	
		Good	Not Good
Cases examined	67	47	20
Hypertrophic "arthritis"	26	16	10
Loss of lordosis	21	10	11
Increased lordosis	3	0	3
Normal curvature	43	35	8
Congenital anomalies	14	6	8
Fusion for anomalies	5	1	4

sults. It becomes apparent from this study that the operation for lumbar disc herniations is not primarily an operation on the disc injury, but an operation on the nerve root or roots involved. Reoperation is a worthwhile procedure if proper notice is taken of this fact and will further reduce an already small group of failures. In addition, knowledge gained by such studies may reduce the number of patients who obtain incomplete relief from surgery, and therefore the number who may need a second procedure.

Particular attention is called to the value of making certain that the

TABLE 4

Symptoms and results of second operation

	Total	Results	
		Good	Not Good
Recurrent sciatic pain alone	26	20	6
Recurrent back pain only	9	2	7
Not fused	5	2	3
Fused	4	0	4
Recurrent sciatic and back pain	58	45	13

TABLE 5

Results of technical procedures

Technical Procedures	Total	Good Results
Generous decompression of nerve root	33	27
Nerve root section	15	10
Chordotomy unilateral	2	2
Removal of new herniation	16	12
Removal recurrent herniation	17	17
Spinal fusion	15	6
No fusion	52	41

TABLE 6

Miscellaneous factors and results

Factors	Total	Good Results
Reoperation after a satisfactory interval of relief	21	17
Reoperation where insufficient relief obtained at first operation	46	30
Compensation cases	23	10
Non-compensation cases	43	35

Reoperated cases: average age 38.4 years.
Cases not reoperated: average age 39.9 years.

TABLE 7

Results of all cases reoperated

	Total
Cases reoperated	67
Results	
Good or excellent	47
Improved	17
Unimproved	3

opening through which the nerve root must pass be at least 50 per cent larger than the root itself; also that there be no loose pieces of cartilage left behind, above, or below the interspace, attached to the nerve root or in the intervertebral foramen, and that no nuclear material be left in the intervertebral space. Bony prominences should be removed, or, better, gently hammered down. The results of nerve root section are fairly good. The success of fusion is unimpressive; fusion nevertheless should be done if no other direct approach seems reasonable. The worst results were obtained in those cases in which there was persistent or recurrent back pain without sciatic pain. The effect of compensation is becoming of increasing importance. It should be noted that in compiling statistics in this study, no postoperative result was classified as good unless the previous way of life was resumed. Many of the results tabulated as "not good" include improved cases in which reoperation was successful at least to the extent that significant relief was obtained.

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PROCAINE BLOCK OF FRONTAL LOBE WHITE FIBERS AS A MEANS OF PREDICTING THE EFFECT OF PREFRONTAL LOBOTOMY

I. EXPERIMENTAL STUDIES*

ORVILLE T. BAILEY, M.D., WILFRED T. SMALL, M.D., AND FRANC D. INGRAHAM, M.D.

Neurological Institute of the Children's Medical Center, Boston, Massachusetts

WITH AN INTRODUCTORY NOTE BY

WILLIAM P. VAN WAGENEN, M.D.

Strong Memorial Hospital, Rochester, New York

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THE greater one's ability to predict a clinical result, the nearer a procedure approaches a scientific level, supplanting empiricisms and rule of thumb. In no field of medicine has empiricism been more rampant than in the field of major psychiatry, especially in treating borderline disorders. This borderland, now so commonly referred to as psychosomatic medicine, is vast, as any practitioner of medicine well knows, and is one in which complaints of pain play a large part. This and the following paper concern themselves with early study of efforts to predict, in some measure at least, the outcome of the treatment of mental disorders by physical means, such as the division of the white fibers in the frontal lobes of the brain.

As a generalization it may be said that lobotomy has come to be used *first*, where there are relatively pure disturbances of one or more of the basic emotions, whether the patient is psychotic or not; *secondly*, where "the personality is split" and where disturbance of the emotions exists to any particular degree, especially if nursing is a major problem; *third*, as a means of creating an unconcern or unawareness of pain caused by known organic disease, such as terminal carcinoma; *fourth*, in the treatment of certain psychomotor fits or epileptic equivalents; and *fifth*, in psychopathic states, where it has yielded indifferent results.

In these five groups, there has not been any adequate means of predicting a result except by the comparison of one patient with some other patient who appeared to have symptoms similar to the patient in question. This method of selection of patients for treatment may be pardonable when the procedure is a reversible or a relatively harmless one. However, lobotomy is most decidedly an irreversible procedure. Once white fibers of the central nervous system are divided, they are gone for all time.

Some months ago, the thought occurred to me that one might be able in certain cases to predict the result of frontal white fiber section by a procaine block of those fibers.

It is well recognized and fully appreciated that not all patients having

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a lobotomy obtain an immediate response. Months may elapse before the final degree of improvement is reached. In painful states, both secondary to known organic disease and to disease of unknown origin—as many facial pains—a result can be more quickly determined with reasonable accuracy. The effect upon abnormal hyperactive states can also be evaluated in a short time, as a general rule. The release from states of mutism and catatonia can seldom be predicted in advance of operation by the use of a novocain block.

Procaine has been used by many of us at the time of cerebral operations to block the fibers from the motor cortex. In 1939, Donaggio[1] advised procaine injections into the frontal lobes as a therapeutic measure. He did not give any case reports nor any statement regarding the effect of such injections if he actually carried them out. This is the only reference thus far uncovered to such a procedure, either from a diagnostic or a therapeutic point of view.

Before making extensive clinical trials, it seemed advisable to find out whether injections of procaine caused significant damage to the white fibers at the site of injection and to determine in the laboratory what possible dangers might be encountered. The next step was to correlate the experimental results with trial in clinical patients. An integrated program was therefore set up, the animal experiments being done in Boston. The clinical studies were carried out at the Veterans Administration Hospital in Canandaigua, New York. The patients selected were the severe and usually degenerated or disturbed psychotics. A few patients with facial pain were observed at the Strong Memorial Hospital.

WILLIAM P. VAN WAGENEN

MATERIALS AND METHODS

An attempt was made to simulate the conditions in patients as nearly as was possible in experimental animals. The material injected was procaine hydrochloride (U.S.P.) in 1 or 2 per cent aqueous solutions, prepared fresh at frequent intervals. Twenty-two cats weighing 2–4 kg. each received injections of procaine in the frontal white matter. In 9 others a sterile solution of sodium chloride (0.85 per cent) in water was injected to provide control material. A preliminary series of 8 cats received the procaine solution mixed with trypan blue to make a final concentration of 0.04 per cent of dye. It was hoped that the trypan blue would give some indication of the area in which the injection mass spread. The results clearly marked the area of trypan blue diffusion but it was open to question whether the spread of procaine bore any relation to that of trypan blue. This approach was immediately abandoned in favor of a chemical technic to be described later. A few monkeys were also used to clarify special points and for comparison.

Technic of Injection. Anesthesia was induced with veterinary nembutal, 25 mg. per kg., given usually intravenously or occasionally by the intraperitoneal route. By measurements made at autopsies on cats, it was possible to place the injected

material in the frontal white matter of the cerebral hemispheres of cats with considerable accuracy. A 2 cm. midline incision was made to expose the coronal suture. A $\frac{1}{8}$ inch hand-drill hole was made in the calvarium 1 cm. lateral to the midline on either side and 2 mm. posterior to the coronal suture. The use of bone wax to prevent reflux proved to be a detriment rather than an advantage. Reflux was kept to a minimum since the needle stump fitted snugly and compressed the subarachnoid space at the site of injection without the use of extraneous material. One-half ml. of the solution was then injected slowly from a 2.0 ml. syringe through a #25 needle 1 cm. long with blunt end. The needle was directed vertically while the animal's head was held in an upright position. The needle was left in place for a few seconds before removal. The wound was closed in layers with interrupted silk except in those animals that were to be sacrificed less than 1 hour after injection.

Pathological Technics. For the study of injury to cells and fibers in the brains of the experimental animals, the brains were fixed in toto in 10 per cent formalin. Histological technics used were hematoxylin and eosin, phosphotungstic acid hematoxylin, Bodian's method for nerve fibers and sudan black for myelin.

CHEMICAL STUDIES

It was apparent that the extent of procaine spread could be determined only by a chemical reaction involving the procaine molecule. The following criteria were used in seeking a satisfactory method:

1. The chemical reaction must be specific for the procaine molecule.
2. The tissue must be fixed in such a manner that postmortem diffusion would not occur or would be reduced to an absolute minimum.
3. No solution should be used which would allow a shifting or diffusion of procaine.
4. The reaction product must be intensely colored so as to be readily seen.
5. The reaction must be sensitive to very small amounts of procaine.

Though many color reactions for the detection of procaine have been described, only once before to our knowledge has an attempt been made to locate procaine in nerve tissue.[3] The tissue was passed through various chemical solutions and no attempt was made to inhibit postmortem diffusion. Fulton[2] in 1921 located procaine in tissue while working on the physiology of local anesthetics, but here again the method involved transfer of tissue through solution.

In 1926 Riegel and Williams[4] described a color reaction for procaine which they used as the basis for a colorimetric method to detect it in solution. The reaction as described by them is shown in Fig. 1. It was found that this method could be modified to suit our purposes. By placing the specimen for a few seconds in the nitrous acid vapor produced by the reaction of HCl and $NaNO_2$, the procaine in the tissue could be diazotized. The tissue was then placed in NH_3 vapor given off by an open jar of concentrated NH_4OH. The presence of procaine was indicated by an intense orange-yellow color (Fig. 2). The reaction can also be obtained by volatilizing certain other compounds, including β-naphthol.

COLOR REACTION FOR THE DETECTION OF PROCAINE

(E.R.Riegel and J.F.Williams 1926)

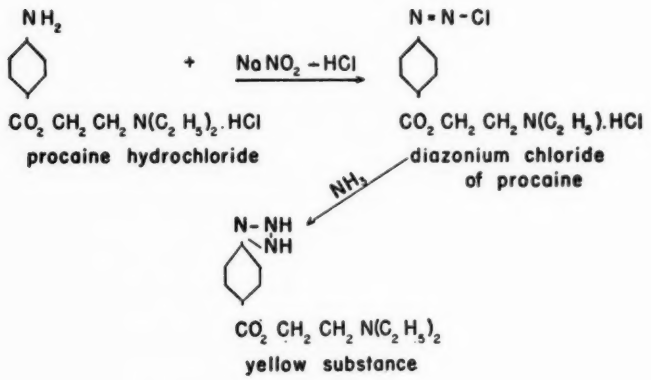
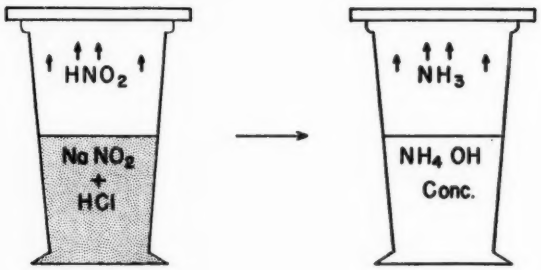


FIG. 1.

Coronal sections of brain which had been injected with procaine were cut from the frozen specimen 2.0 mm. thick with a sharp razor. These were placed on slides and treated with the vapors described. The exact site of the

COLOR REACTION FOR DETECTION OF PROCAINE IN TISSUES

(Riegel, Williams reaction modified)



By holding tissue to be tested on slide over two staining jars as shown, the volatile nitrous acid and ammonia vapors are sufficient to bring out reaction product in the tissue if present.

FIG. 2.

procaine could readily be identified by the yellow-orange color produced. Uninfiltrated normal brain did not change. The intensity of color did not fade for several hours.

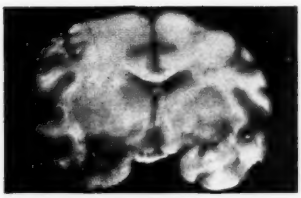


FIG. 3

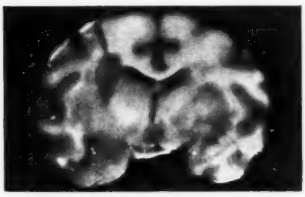


FIG. 4

FIG. 3. Monkey's brain injected with procaine just after death. The color reaction has not been applied.

FIG. 4. Brain shown in Fig. 3 after color reaction.

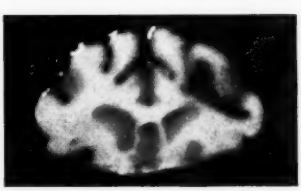


FIG. 5

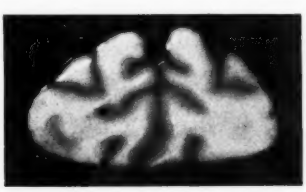


FIG. 6

FIG. 5. Cat's brain 5 minutes after procaine injection. The area of procaine infiltration is shown by the color reaction.

FIG 6. Cat's brain 30 minutes after procaine injection. The color reaction is very pale, indicating that most of the procaine has been absorbed.

The reaction is sensitive to as little as 0.00045 mg. of procaine per cc. It is also specific for procaine and other local anesthetics and does not produce a color reaction with any normal constituent of brain tissue. By using only materials in the gaseous state, the specimen does not touch any solution, thus completely avoiding spread of procaine in the course of the reaction. Rapid freezing of the brain specimen was used to prohibit postmortem diffusion. This was done by placing the specimen in a Petri dish in contact with a bath containing alcohol and dry ice in bubbling equilibrium. We have been unable so far to detect procaine in microscopic sections (4–16μ in thickness) prepared in a Lindeström-Lange box. This is probably due to the extremely low concentrations of procaine in a single tissue slice. While we have not used this method on tissues other than brain, it would seem to be applicable more generally, since the interfering substances are not commonly found in living organisms to any extent.

RESULTS

I. *Cats Receiving Procaine Injections in the White Fibers of the Frontal Lobes.* In 22 cats, 0.5 ml. of 2 per cent procaine was slowly injected into the white fibers of one frontal lobe in order to determine the extent of local spread, the time of disappearance, and the tissue changes produced. Two cats were sacrificed at each of the following intervals after injection: 5, 15, 30 and 45 minutes; 1, 2, 6, 12, 24 hours; 1 and 2 months.

The extent of local spread and the time of disappearance were followed by the reaction previously discussed (Figs. 1 and 2). As a control, a normal monkey's brain was injected just after the monkey had died. Fig. 3 shows the brain before carrying out the reaction and Fig. 4, the result of its application. The region of procaine infiltration is brilliant yellowish-orange while the rest of the brain has not changed color.

In the cats sacrificed 5 minutes after injection, the procaine was found to have infiltrated the white matter beyond the site in which it had been injected, while the gray matter was less involved (Fig. 5). The colored area measured approximately 7×4 mm. This is an average measurement; the size of the area varied somewhat with the technic, especially the speed of injection. No instances of spread beyond the frontal lobe were encountered at any of the time intervals studied, though a minimal increase in the size of the yellow area could be detected at the intervals studied up to 30 minutes (Fig. 6). The reaction for procaine was obtained in all animals sacrificed 30 minutes or less after injection, in one animal at 45 minutes and not at all at longer intervals. Within less than 1 hour, then, there was no longer sufficient procaine at the site of the injection to give even this sensitive reaction.

When the injected frontal lobes were studied microscopically, the needle tracks could be easily followed down to a space at the tip, where the procaine had been injected. In the specimens obtained 24 hours or less after injection, the nerve fibers could be seen pushed apart over an area corresponding in size to the yellow zone seen after the chemical reaction had been applied.

Fragmentation of nerve fibers was confined to a narrow zone at the margin of the space. There was no polymorphonuclear leukocytic infiltration, but a slight increase in microglial nuclei could be made out. The astrocytes and oligodendroglia appeared unchanged. At 1 and 2 months after injection, the space had decreased in size but was still clearly visible. The number of microglial nuclei was slightly increased about the space. Occasional large astrocytes were seen in this area but the numbers of astrocytes and oligodendroglia were within normal limits. There was no degeneration of nerve fibers except in a narrow zone about the space, where they had largely disappeared. In a small area about the space, loss of myelin was demonstrated; this averaged 3×2 mm. in paraffin sections. The damage to cerebral tissues by the procaine solution was almost identical qualitatively and quantitatively with that produced by the injection of the same amount of normal saline (see below).

II. *Cats Receiving Normal Saline Injections in the White Fibers of the Frontal Lobes.* In 9 cats, 0.5 ml. of normal saline (0.85 per cent sodium chloride in water) was injected into the white fibers of one frontal lobe. These served as controls for the series receiving procaine injections, the only variation in technic being the difference in solutions. The cats were sacrificed at the following intervals after saline injection: 5 and 15 minutes; 1, 2, 6, 12 and 24 hours; 1 and 2 months.

When the frontal lobes of these cats were examined microscopically, a space of the same size and character was found at the point of injection as was present when procaine was used. The character and amount of cellular reaction as well as the degree of nerve fiber disruption was essentially the same as with the procaine injections at all time intervals compared. The same was true of the loss of myelin in the animals allowed to survive for 1 or 2 months.

III. *Animals Excluded from Series I and II.* At the beginning of this study and before the operative technic had been fully worked out, several cats died instantly when the procaine had been injected. In each of these, it was found that the procaine had been allowed to escape into the subarachnoid space or the ventricular system or both. With further experience, this complication was not encountered.

No deaths resulted in the series of saline injections.

Procaine injections into the frontal white fibers were carried out in a few monkeys with the same results as were obtained in cats. Since no additional information could be obtained, a larger series was not undertaken.

DISCUSSION

The precise mechanism by which local anesthetics produce their effects is still unknown. However, since transmission of nerve impulses can be blocked by such local anesthetics as procaine, this might be true of fibers within the brain itself. Thus, if procaine could be injected into the brain in proper concentrations, interruption of activity in the area injected would result. To be of clinical value, the procedure must cause no serious systemic effects or significant tissue destruction at the site of injection.

The injection of procaine solution into the frontal white fibers has been accomplished safely in cats and monkeys. No untoward general reactions were detected unless the solution was inadvertently allowed to enter the subarachnoid space or ventricular system. When this occurred, an immediate fatality resulted. With improved technic, this complication was entirely obviated. The total volume of the cat's brain is so small that accurate injection of fluid is far more difficult than it is in larger animals. Escape of procaine was not encountered in the experiments on monkeys. The margin of safety in man should be still greater.

As estimated by the color reaction, all the procaine had disappeared from the site of the injection in less than 1 hour. It proved impossible to determine what changes the procaine brought about in cerebral activity because the effect of the anesthesia persisted throughout the time the color reaction could be demonstrated.

Histological evidence of residual tissue damage due to the procaine was slight. It was about the same as that produced by the injection of an equal volume of normal saline and only slightly greater than that of the needle track alone. From the experimental evidence, therefore, serious permanent damage to structures in the region of injection would not be expected.

These studies were not designed to determine the clinical value of procaine blocks of the frontal white fibers but were planned to determine its safety. The procedure was regarded as safe for use in human patients, insofar as could be ascertained in animal experiments.

SUMMARY

1. Procaine in 2 per cent solution was injected into the frontal white fibers of cats and a few monkeys.

2. A color reaction for the demonstration of procaine in tissue is described. Since the reagents used are in the gaseous state, this technic obviates errors resulting from the spread of procaine by test solutions.

3. As judged by this reaction, local diffusion of procaine solutions is minimal in the frontal white matter and disappears in less than 1 hour.

4. Histological evidence of residual damage is slight; tissue changes are no greater than those caused by the injection of the same amount of normal saline solution.

5. Escape of the procaine solution into the subarachnoid space and the ventricular system is a most serious complication but can be avoided by controlled technic.

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PROCAINE BLOCK OF FRONTAL LOBE WHITE FIBERS AS A MEANS OF PREDICTING THE EFFECT OF PREFRONTAL LOBOTOMY

II. CLINICAL EVALUATION

WILLIAM P. VAN WAGENEN, M.D.,* AND C. T. LIU, M.D.†
Veterans Administration Hospital, Canandaigua, New York, and the Strong Memorial Hospital, Rochester, New York

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IN THE introductory note to the paper by Bailey, Small, and Ingraham,[1] reference has been made to the use of lobotomy in certain disturbances and aberrations of the emotions.

The basic emotions in man have been variously classified. The following is a working list of our own that can be recorded if not measured accurately.

1. Fear and awe	—of falling
	—of certain animals
	—for self and of self
	—for others and of others
	—for excesses of normal stimuli as light, sound
2. Pleasure	—referable to the vegetative nervous system, skin, and mucous membrane areas by,
	—mild usual stimuli such as rubbing the skin, warmth, vasodilation, and peristalsis
	—referable to special senses as
	—vision
	—hearing
	—taste
	—referable to function (work and play)
	—for possession
3. Anger and rage	—toward self
	—toward others
	—toward functions of work and play
	—toward inanimate objects
4. Love	—of self
	—for others
	—for function (work and play)
	—for possessions
5. Sorrow, pity and loss	—for self
	—for others
	—for functions (work and play)
	—for possessions

The seat of primitive emotions appears to be in the thalamus. Motor reactions and responses to primitive emotions originate primarily in the

* Consultant in Neurosurgery, Veterans Administration—Area 1.
† Attending Neurosurgeon, Veterans Administration Hospital, Canandaigua, New York.

hypothalamus and caudate nucleus. As development of the brain has taken place, functions of the thalamus and caudate nucleus related to emotion have been moved out, in part, to field stations in the frontal and probably the anterior temporal lobes. For this reason, we have come to associate the frontal and temporal lobes of the brain with disturbance and alterations of the emotions. It may be said that the more the emotion is limited to the thalamus alone, the more constant and stereotyped is the pattern of response by the motor component of the old brain. The more the emotional response is delegated to the frontal or temporal lobes, the less predictable and more varied is the pattern of the response.

The average curve of the rise and fall of the "intellect" as opposed to the emotional state of normal man is a fairly smooth one. The curve of the intensity of man's various emotions differs both with age and with the individual emotion. As a generalization, one may say that in the younger years, fear and pleasurable emotions are highest; with love, sorrow and pity relatively low. After mid-life, these two tend to merge and then change places. When the emotions fail to follow in a general way the usual curve, so called mental disturbances result.

Fear is the emotion most apt to take an upswing in the latter years when it normally is regressing. There are a number of attributes of any emotion. One is the fact that an excess of any one crowds out all others for the time being, at least. Secondly, an excess of any emotion calls for action of one sort or another. The action may be positive or negative, acceptable or not to society or environment.

In summary, the use of lobotomy has come to be directed toward problems where there has been a disturbance of the emotions and not the intellect. Fear is the outstanding emotion and one most often disturbed. Fear of self, others, pain, name calling, hallucinations, etc. are examples. Long-continued disturbance of the emotions usually leads to deterioration of the intellectual functions.

The technique of injection of procaine into the frontal lobe white fibers has varied from the start and is not yet an entirely settled affair. Our present plan is to make two small burr holes, under local anesthesia if possible, over the frontal poles of the brain, or just anterior to the coronal suture bilaterally. The pia and arachnoid are sealed to the underlying brain by means of the coagulating current of an endotherm machine. A period of several days is then allowed to elapse. This procedure is designed to accomplish two things. First, to minimize return of the procaine into the subarachnoid space along the needle tract, and secondly, to note the effect of a nonspecific surgical procedure. The novocain injections are made, whenever possible, in the patient's room or familiar surroundings. Certain disturbed pyschotic patients have to be given a small dose of sodium pentothal intravenously and observed as soon as the effect wears off. One usually has a matter of a few hours to note an effect of a novocain block. Two per cent procaine is being used most of the time, 3 cc. per side, injected very slowly with a very

fine needle. Injection of novocain into the ventricle may have very serious consequences. Leakage of novocain into the cortical subarachnoid space was thought to have occurred in one case, with alarming results, i.e. coma and convulsions. If in doubt as to the location of the needle, a small amount of air may be injected into the ventricles. A lateral X-ray plate will show the relationship of the needle to the ventricle. The diffusion of procaine in white matter is known to be rapid and extensive.

SELECTION OF CASES AND SCOPE OF STUDY

The patients selected for novocain block were divided into a psychotic and nonpsychotic group. Members of the former group were all badly disturbed patients at the Veterans Administration Hospital in Canandaigua, New York. They all had been passed by the Lobotomy Board as suitable for lobotomy according to rigid standards set up by a National Board. On the whole, they were considered for lobotomy mainly because they were such serious nursing problems, because of aggressiveness, assaultiveness, suicidal tendencies, etc. One was selected in the hope that reduced activity would aid in the treatment of pulmonary tuberculosis. It may well be that a distinct percentage of psychotic tubercular patients may profit greatly by this measure. The same might be said of the psychotic patient suffering from intractable peptic ulcer.

The nonpsychotic group were those selected from a neurosurgical practice because of severe disabling hypochondriasis or complaints of pain or because of nursing problems.

CASE REPORTS

PROCAINE BLOCK OF FRONTAL LOBE WHITE FIBERS IN 20 PSYCHOTIC PATIENTS

Case 1. No. 4057 C.V.A. L.S., a 54-year-old veteran, began to show symptoms of mental illness while being treated for peptic ulcer 8 years ago. The diagnosis then was that of an "involutional melancholia." Gradually there developed full symptoms of schizophrenia, characterized by episodes of violence, assaultiveness, destructiveness, and hyperactivity. His speech was consistently obscene. He had experienced auditory hallucinations and paranoid delusions. Adequate electric shock therapy did not give lasting improvement. He required frequent sedation and restraint.

A novocain injection into the frontal lobes was done under pentothal anesthesia on March 16, 1949, at 9:00 A.M.; $2\frac{1}{2}$ cc. of 1 per cent novocain were used on each side. When he awoke, he talked in a whisper and seemed much quieter than before. He slept through the night quietly and next morning he was quite pleasant and cooperative. By the afternoon, or about 24 hours after the injection, he was again obscene, hyperactive and manneristic.

A second injection was done on April 7, 1949, again under sodium pentothal; 3 cc. of 1 per cent novocain were injected bilaterally. This time, there was practically no period of improvement. He was hyperactive, overtalkative and hallucinated within 1 hour after injection.

The results of these injections were not considered conclusive and suggested

that a lobotomy would not change his behavior. However, because the patient was such a severe management problem, a bilateral lobotomy was done on April 14, 1949. A 5½ cm. cut anterior to the ventricles was made bilaterally. Almost immediately on recovery from anesthesia, he became obscene and rambling in his speech. He was incontinent for a few weeks. He was confused and hyperactive for 3 weeks and then suddenly became docile for about 2 weeks. During the 13 months since lobotomy, however, he has shown no consistent clinical improvement, being hyperactive, noisy, uncooperative and sometimes assaultive. He would not take part in the "push program." Finally his ward physician reported to giving him intermittent electric shock treatments on a p.r.n. basis.

SUMMARY. *First injection of novocain gave questionable improvement in behavior for 24 hours. Second injection gave no improvement. Lobotomy has given no consistent improvement up to 24 months.*

Novocainization in this case seemed to have suggested the correct result from lobotomy.

Case 2. No. 3467 C.V.A. F.B., a 35-year-old man, became mentally ill at the age of 22 years when he complained that his wife was trying to kill him. Dementia praecox was diagnosed. Commitment was advised but was refused by the family. He entered the Navy in 1943 and within 1 year, he was again in a mental hospital. He was discharged from the Navy in 1944 with the diagnosis of dementia praecox, improved. He continued to do poorly however, and was admitted to V. A. Hospital, Canandaigua, in 1945.

On admission he was surly, overactive, noisy, hallucinating and mentally deteriorated. He was given two courses of electric shock treatment. There was no improvement and re-evaluation in May 1949 showed him to be dull and indifferent most of the time, with unpredictable bursts of aggressiveness and suicidal attempts. His speech was mumbled and the contents were rambling, irrelevant and incomprehensible.

First novocainization under a small amount of sodium pentothal anesthesia was done on May 10, 1949; 5 cc. of 1 per cent novocain were used on each side. When he awoke from anesthesia he appeared mentally confused for about 2 hours and answered questions slowly and irrelevantly. Then he suddenly cleared up and was in good contact for about 48 hours, during which time he answered questions clearly. He appeared to present the "startle reaction," waking up with an unusually startled expression when touched. After 48 hours he again became seclusive, withdrawn and hallucinated.

A second novocainization under local anesthesia was done on May 13, 1949. He showed improvement for 12 hours.

This patient was examined by a psychologist approximately 24 hours after the first novocainization and 1 hour after the second novocainization. After the first injection, his memory functions were approximately the same as before. In drawing figures, it was noted that anxiety and delay were much more evident than before. After the second injection, he seemed quieter from the psychomotor point of view. He responded to his hallucinations and talked to himself more freely. In general, his delusions and hallucinations did not disturb him as much, as he was able to express himself more clearly. His memory function seemed improved.

A lobotomy was done on May 17, 1949. Two months later the examiner reported great improvement, i.e. "tone of voice was normal, speech was clear, expressions

were more spontaneous." Voices were still telling him to break windows or injure himself; "I don't obey them any more because I have more will power." He was then assigned to occupational therapy, where he did excellent work.

The auditory hallucinations diminished or at least he denied them about 9 months after lobotomy. His general behavior is, on the whole, pleasant and cooperative. However, he has periods of silliness and will heckle other patients, especially negroes. Twelve months after lobotomy he had improved so much that he was sent home on a trial visit in the custody of his brother.

He obtained work as a mail clerk in a warehouse. He made an excellent adjustment and after several follow-up examinations at the Psychiatric Clinic of the Veterans Administration Regional Office in Buffalo, New York, he was discharged on May 22, 1951.

SUMMARY. *Deteriorated, seclusive, schizophreniac with mumbled speech and auditory hallucinations. Novocainization seemed to be associated with an improved mental state for a brief time. Lobotomy has also produced encouraging results up to 24 months.*

Case 3. No. 2712 C.V.A. S.B., aged 26 years, began to have symptoms of mental illness about 2 months after induction into the Navy in 1943. He became mute, unresponsive, negativistic, resistive, seclusive, and at times threatening and assaultive. He has been in mental hospitals ever since. One course of electric shock therapy failed to produce any lasting improvement. Re-evaluation in May 1949 showed him to be dull, indifferent, passive and emotionally deteriorated. He displayed facial grimacing and mumbled to himself. He spoke only in short staccato sentences—"yep," "no," "don't know," and "pretty good." At times, however, he would suddenly become destructive and assaultive. The diagnosis first considered was a catatonic type of schizophrenia, but later his behavior seemed more like that of a hebephreniac.

The first injection was done with 1 per cent novocain. Five cc. in each frontal lobe produced no change in his responses to questions. He remained seclusive and mute.

A second injection of 8 cc. of 1 per cent novocain into each frontal lobe again produced no changes.

The third injection was done with 4 cc. of 2 per cent novocain in each frontal lobe. He perspired excessively during the procedure, but when the procedure was ended, he showed no change in his behavior. Because the novocainizations were done at a time when he was not disturbed, we could not predict his behavior in that respect.

Lobotomy was done on May 23, 1949. At the present time, 12 months after operation, he is still childish, deteriorated, lacks initiative, and needs constant supervision. However, he has shown no more assaultive or hyperactive episodes. His father has wanted to take him home. The home situation is unfavorable and the staff does not feel that he would be able to adjust outside the hospital. The patient is still incontinent at times and has had several generalized convulsions which have been controlled by phenobarbital.

SUMMARY. *A hebephrenic schizophreniac who was usually mute and withdrawn with unpredictable outbursts of hyperactivity was given 3 novocain injections in varying strength and amounts. This produced no change. Lobotomy has stopped his hyperactive episodes but has produced no improvement in his general mental condition up to 24 months.*

Case 4. No. 5803 C.V.A. H.C., aged 25 years, had symptoms of schizophrenia for 5 years. Two series of electric shock therapy gave little improvement. A topectomy was done at the Bronx V.A. Hospital on Sept. 28, 1948. This produced improvement in his behavior for about 3 months. Then he became increasingly restless and tense. There were episodes of assaultiveness and one attempt at suicide. Mental status on June 8, 1949, was that of a highly disorganized individual with a rambling conversation and incoherent ideas.

On the night of June 27, 1949, the patient suddenly jumped up from bed and ran into the day room. When an aide tried to stop him, he struck the aide in the face, saying "That's for you, you SOB of a farmer, I'm getting out!" He was placed in a restraint sheet. The next morning he still appeared to be tense and high-strung.

Five cc. of 1 per cent novocain were injected into each frontal lobe. Physiological responses were excessive perspiration, nausea and vomiting. The patient stated that "he did not feel any different." Objectively, he appeared quieter and more contented. This lasted for about 1 hour. He behaved quietly for 2 days. On July 1, 1949 he again became hyperactive, pacing constantly and talking continuously.

A second injection of 5 cc. into each frontal lobe was given. Unfortunately, about 5 minutes after the injection, generalized convulsions occurred which lasted for about 3 minutes. Sodium amytal was given and he remained quiet the rest of the day.

A bilateral prefrontal lobotomy was performed on July 7, 1949. Almost immediately after the operation, there was a marked change in his behavior. He became friendly and cooperative. Psychological tests were done 2 months after lobotomy. These tests showed evidence of greater control of behavior. Aggressive behavior, and impulsive behavior was less. There was a loss of distortion in speech and in written language. There was greater perseverance and tenacity in goal. A minimal increase in spontaneity and relationships with others was noted. He appeared apathetic and depressed at times. The changes were so encouraging that on the third month after operation he was sent home on a trial visit. He made a good adjustment at home and found a job in a rubber factory. Adjustment was satisfactory up to 10 months after lobotomy when he had an altercation with his boss in the factory, became very hyperactive and had to be sent back to this hospital. At present, 23 months after lobotomy, his condition is still poor.

SUMMARY. *Young schizophreniac. Behavior characterized by unpredictable assaultiveness, disorganized speech and subdued tension. Topectomy gave temporary improvement. Results of novocain block were encouraging, although not conclusive. Lobotomy produced marked improvement for about 9 months, then a relapse in the 10th month postoperative.*

Case 5. No. 250 C.V.A. A.F., a 56-year-old man, has been in this institution for 26 years with a diagnosis of dementia praecox, hebephrenic type. He was found to be suffering from pulmonary tuberculosis 8 years ago. The process is still active. Because of the tuberculosis, he had not had any shock therapy. His behavior was characterized by repeated attempts at self-injury, such as banging his head against the walls, scratching his skin till it bled, and rubbing his heels. Most of the time he was confused and incoherent. Because of his tendency at self-injury he has been in restraints almost constantly and had to be tube-fed constantly.

After the first injection of 4 cc. of 1 per cent novocain, which was done under pentothal, the patient was able to be free from restraints of any sort. He immediately started to feed himself and showed no tendency to hurt himself. Speech was clear

and coherent most of the time. This effect lasted about 24 hours. Then his speech became garbled and incoherent again. He would roar with laughter for no reason. On the 3rd day, he again began to bang his head and had to be placed in restraints.

The second novocain injection was done during one of his impulsive attempts to hurt himself. Five cc. of 1 per cent novocain were injected into each frontal pole. Almost immediately after injection, he began to beat his ankles together, so that novocainization apparently had given him no improvement. Then for 2 weeks he surprised everybody by behaving very well. He played the piano, appeared to be more alert and responded readily. He fed himself and ate heartily. He gained weight.

After these 2 weeks of encouraging remissions he suddenly relapsed. He tried to hurt himself by sticking his hand into an electric fan, became hyperactive, crawled on the floor and lost his appetite. A third injection of 5 cc. of 1 per cent novocain was done under local anesthesia on Aug. 2, 1949. This failed to produce any dramatic results. In other words, novocainization gave apparently some improvement the first time but failed on two latter occasions.

A lobotomy was done under local anesthesia on Aug. 9, 1949. For about 6 months the results were very gratifying. He lost his self-abusive and suicidal tendencies. His mental status greatly improved and he gained 8 lbs. in 2 months. His pulmonary condition did not show any great change. He was allowed to do light work on the ward. At 9 months after operation, he showed no great improvement in his mental condition, but this is not surprising in view of his long hospitalization. He still bangs his head and scratches his skin now and then, but has not required any sedation or restraint. Examination 22 months after operation showed further mental deterioration.

SUMMARY. *Schizophreniac with pulmonary tuberculosis, whose behavior is characterized by compulsive tendency to injure himself, requiring constant restraints in last 3 years. Novocainization gave very clear-cut improvement on one occasion, but was poor on two later injections. Lobotomy produced good improvement for a short while, but now after 2 years, he is classified as a poor result.*

Case 6. No 4500 C.V.A. H.L., aged 24 years, has had schizophrenia for 3 years. His behavior was characterized by continual hyperactivity, assaultiveness, destructiveness, obscenity and constant overtalkativeness. Two courses of electric shock therapy in the past had produced brief remission. For the last 6 months before operation, however, he had been in sedation packs daily, camisole sedation nightly, and required maximum nursing supervision. He was entirely inaccessible to any psychological approaches because of his hyperactive talkativeness.

On Aug. 8, 1949, 4 cc. of 1 per cent novocain were injected into each frontal pole. A wax recording of the patient's speech was made during the operation. After the first cc. of novocain injection, the patient's speech immediately slowed down. Unfortunately, he began to show twitchings of his face and hands. A portable x-ray of the skull showed that the needles were pointed too far posteriorly. The needles were replaced more anteriorly and 3 cc. more of 1 per cent novocain were injected. Two-tenths gm. of sodium amytal was injected intramuscularly when the twitchings first appeared. This sedation did not seem to alter the patient's speech. Following the injection of the novocain, however, his tone of voice definitely became lower, his rate of speech became slower and he appeared under less tension. This effect lasted only about 1 hour.

A second novocainization was done on Sept. 12, 1949. Four cc. of 1 per cent no-

vocain plus 1 cc. of 2 per cent novocain were injected bilaterally. A wire recording made at this time showed that his speech again became slower and lower. The results were not as remarkable as the first time.

A third novocainization was done on Sept. 14, 1949, with 4 cc. of 2 per cent novocain bilaterally. The results were poor. The patient paused for breath for a few seconds and he showed some slowing of speech for a few minutes during the injection, but towards the end, he became very restless and speech became wilder.

The results of the novocainization, as a whole, led us to believe that lobotomy should produce at least moderate improvement in the hyperactivity of his speech. There was nothing to suggest that the contents of his speech would be normal or that his basic psychosis would be altered.

Lobotomy was done on Sept. 16, 1949. A wire recording of his speech was taken during the operation. His voice again showed a dramatic drop as the last quadrants were cut. During the first 3 months after operation there was a remarkable improvement in his speech and behavior. He would soil and wet himself occasionally but he no longer needed heavy sedation or packs continually. The improvement continued so that it was possible to transfer him from the disturbed ward to a quieter ward. His rehabilitation gradually progressed so satisfactorily that he was sent home on a "trial visit" on Sept. 3, 1950. He obtained a job as a laborer for the shops of the Pennsylvania Railroad and has been making satisfactory social and economic adjustment to date.

SUMMARY. *A completely inaccessible hyperactive, assaultive and overtalkative schizophreniac. Novocainization on two occasions produced definitely favorable improvement. A third injection was not so favorable. Results after lobotomy have been very gratifying up to 9 months postoperative.*

Case 7. No. 5884 C.V.A. J.C., a 37-year-old man, had been suffering from symptoms of paranoid schizophrenia for a minimum of $4\frac{1}{2}$ years. He received both insulin and electric shock therapy 3 years ago.

For a short time before lobotomy here, he was generally well behaved but he would have unpredictable periods of self-mutilation and suicidal attempts. At times he had enough insight to feel that such an episode was coming and he would ask to be placed in camisole. He had delusions of body odor and halitosis and auditory hallucinations. Psychological tests between July 29, 1949, and Aug. 4, 1949 showed that although he was an individual of superior intellectual capacity, he was functioning at an average low level of intelligence because of the psychotic process and because of a concentration defect. Since he was a paranoid schizophreniac who was not completely disorganized as yet, but whose self-mutilation tendency had become a major management problem, it was felt that lobotomy was indicated. It was hoped that lobotomy could help to prevent further disorganization or deterioration. Since this patient was in good contact, he was considered a good subject for investigating the effects of novocainization of the frontal lobes on performance in certain psychometric tests and to see if these results could be maintained by lobotomy.

Preliminary trephination was done on Aug. 9, 1949 under pentothal anesthesia. Psychological testing the next day showed no marked difference in his performance. Subjectively the patient "did not feel different" although full use of the power of suggestion was made.

First novocainization with 3 cc. of 2 per cent novocain was done on Aug. 16, 1949, under local anesthesia. Psychometric tests were tried immediately after injection. He was too restless and disturbed by headache to make this examination

satisfactorily. A battery of tests was given about 4 hours after injection when he felt able to do them. This showed slight improvement in his performance.

Second novocainization with 3 cc. of 2 per cent solution was done on Sept. 13, 1949. He had some dizziness and blurring of vision immediately after injection, but this cleared up soon and testing was done 1 hour after novocainization. Again there was improvement as compared with the pre-operative testing, though not more than after the first novocainization. The tests done were digit span, Woodworth-Wells substitution test, Beta Maze, and Haufmann-Kansanin tests.

A prefrontal lobotomy was then done on Sept. 19, 1949. The patient adjusted well after lobotomy and although he still had hallucinations and delusions of strange body odors he showed no self-destructive tendencies. He was taken off the suicidal ward 3 months after operation. He was started on Manual Therapy and Group Psychotherapy. Psychological tests done about 5 or 6 months after operation showed a marked improvement in the Woodworth Wells substitution test, in the Rorschach and in the learning of substitution tests. The I.Q. improved up to 107. Seven months after operation, on April 19, 1950, he was re-evaluated by the Psychiatric Board who found that he was in good contact and felt that he could be on full privileges. He had no delusions or hallucinations. He had written numerous letters home in regard to plans to work as a painter. He was, therefore, given permission to go home on trial visit under custody of his brother on April 25, 1950. On April 28, 1950 he committed suicide at home with a shot gun. A book entitled, "The Case of the Constant Suicide" was found by his bedside. His family, however, found evidences that he had been planning suicide for a long time.

SUMMARY. *A young man who had shown marked tendency at self-destruction in response apparently to hallucinations. Electric shock therapy gave no improvement. Psychological tests done after novocainization showed improvement. There was marked improvement after lobotomy in the hospital but he committed suicide 3 days after being sent home.*

Case 8. No. 1979 C.V.A. S.R., a 44-year-old man, enlisted in the Army on July 19, 1926, and was discharged on CDD on July 3, 1931. Following his discharge he was arrested for petit larceny and was sentenced to 60 days in jail. While in jail it was noticed that his conduct was abnormal and he was sent to the Mattewan State Hospital. He was transferred to the Rochester State Hospital in 1934. There he was silly, hallucinating and delusional. A diagnosis of dementia praecox, paranoid type, was made. He was seclusive, introspective and hallucinated. He became assaultive and it was necessary to transfer him to a disturbed ward. There he was excited and continuously ran about in a circle, emitting strange animal-like cries. It was necessary to use packs repeatedly. He received much sedative medication. After admission to the Veterans Hospital in Canandaigua, the patient was indifferent to his surroundings. He was mute. He would run in circles around a table, bark like a dog, and then he would go under the table where he would stay for hours. At other times he would sit on the floor and hit his head against the wall until he was told to stop. He would smile broadly at intervals. His facial expressions on the whole were dull, vacuous and silly. No delusions could be elicited because he would not answer questions. He was not assaultive and he did not soil or wet himself.

In summary, the patient was a deteriorated paranoid schizophreniac whose behavior was characterized by mutism and two characteristic behavior patterns. Careful records were kept, consisting of hourly observations and notes for 4 days before operation. These showed that he spent his time doing mainly two things

in the ward. He would either lie flat on the floor under the table or he would squat against the wall banging his head and barking like a dog.

First novocainization was done on Oct. 3, 1949, under local anesthesia, with 3 cc. of 2 per cent novocain through two drill holes in the frontal region. During the injection his face became red; blood pressure and pulse showed no change. On return to the ward, patient sat in a chair, which was a very unusual occurrence for him. He answered questions in a very low voice, then he would get up at times and walk around the room brushing his face. This behavior lasted about 6 hours and then he reverted to the old habit of hitting his head against the wall while squatting on the floor.

Second novocainization with 3 cc. of 2 per cent novocain was done on Oct. 7, 1949, under local anesthesia. Again his unusual behavior was broken up for about 4 to 6 hours. He was able to play games in the afternoon.

Lobotomy was performed on Oct. 10, 1949. He was incontinent and wet and soiled himself constantly for about 2 weeks. Since operation he has not reverted to his abnormal behavior pattern. He is able to take part in ward activities, companion therapy and has worked in the kitchen. Present examination, 9 months after operation, shows the patient to still be a deteriorated schizophreniac, but one who has been able to make excellent social adjustment in the hospital. Psychological examination also showed that he has more control over his feelings, and he is more productive than in the pre-lobotomy state. From the view point of management and behavior, he has shown excellent progress, up to 20 months.

SUMMARY. *A 44-year-old deteriorated schizophreniac who was a management problem because of abnormal behavior patterns. Novocainization on two occasions produced marked improvement. Lobotomy has also produced marked improvement in behavior. Since his sphizophrenic process has been of more than 11 years' duration, no marked improvement in his mental state could be expected.*

Case 9. No. 2766 C.V.A. E.S., aged 29 years, had symptoms of schizophrenia since 1943. He had electric shock treatment in 1944 and in 1945 with very little improvement. He gradually showed signs of mental deterioration and became dull, manneristic, self-absorbed and indifferent. It was difficult to elicit any response from him as he answered only: "I don't know" or "no, no, no" to every question. He had many mannerisms consisting of grimaces, inappropriate smiling and laughing to himself. At times, he would have episodes of hyperactivity and destructiveness. Psychological examination had been impossible because of his poor contact.

Novocainization was done on Nov. 4, 1949. Three cc. of 2 per cent novocain were injected into each frontal lobe. Toward the end of the procedure, he slumped in his chair and moved his feet about as if he were restless. However, he denied any headaches and there was no change in his behavior. He continued to show mannerisms and did not seem to be in any better contacts than before the procedure.

A bilateral lobotomy was done on Nov. 7, 1949. During the first few months after operation, there were no remarkable changes. On re-evaluation 6 months after lobotomy, he was still unproductive and dull, and showed no spontaneity. He tried to play games, but couldn't keep his mind on them. He was very child-like and insight was completely lacking. According to the examining psychiatrist's words: "His state now, compared with that before his operation on Nov. 7, 1949, has been raised above the level of an animal. He now recognizes and talks to his mother which he did not do before. He has been home on leave and it is possible that if he continues to go along as he is now, he might, in a period of time, adjust on the outside." After

a short period at home, however, he was returned to the hospital and has shown no further improvement.

SUMMARY. *A deteriorated catatonic schizophreniac who responded very poorly to electroshock treatment. One novocainization did not bring him out of this catatonic state and did not change his behavior externally. Lobotomy has given very little improvement in 19 months.*

Case 10. No. 5264 C.V.A. T.S., a 23-year-old veteran, showed symptoms of schizophrenia in June 1947, and had to be hospitalized on July 8, 1947. He had extensive courses of electroshock therapy, insulin shock therapy and narcosynthesis. All these treatments gave him only temporary relief. He has had many episodes of self-destructiveness and impulsive assaultive episodes. On one occasion, he attempted to kill one of the aides. Then he gradually became seclusive, self-absorbed, mute and withdrawn. Often, he refused food and had to be tube-fed. Psychometric studies were impossible because of his catatonic state.

On Nov. 15, 1949, during one of his episodes when he refused food, 3 cc. of 2 per cent novocain were injected into both frontal lobes. The results were very encouraging. The patient became talkative and responded to questions with coherent answers. He ate his dinner after novocainization and seemed to be in better contact. On Nov. 17, 1949, 3 cc. of saline were injected into both frontal lobes. This did not produce any remarkable results but it was hard to evaluate because the patient was already in pretty good contact before the injection.

On Nov. 18, 1949, a second novocainization with 3 cc. of 2 per cent novocain was done. The results were very encouraging. The patient was able to give a very revealing interview to his ward physician.

On Nov. 21, 1949, a lobotomy was performed. Almost immediately after the operation, the patient became cooperative and placid. His behavior improved so rapidly that he was taken off the observation list within 1 month's time. He worked in the metal-artcraft shop and did excellent work. Re-evaluation 4 months after operation showed that he was in good contact, and well oriented in all spheres. He denied hallucinations. He did not have any true insight into his condition and his judgment was still impaired. He had very little initiative. Because of his excellent behavior, however, it was possible to send him on trial leave 4 months after operation. He has been home up to 21 months after operation but he has been unable to secure work.

SUMMARY. *A catatonic schizophreniac who had shown no lasting improvement with electric or insulin shock. At times he would become mute and refuse food. Novocainization on two occasions brought him out of his catatonic stupor. Lobotomy produced satisfactory results so that he has been able to be sent home on trial visit and has been adjusting well up to 21 months.*

Case 11. No. 3252. W.L., a 37-year-old man, has had symptoms of catatonic schizophrenia for 6 years. He received both insulin shock and electroshock therapy with only slight improvement for a short time. Evaluation in March 1949 showed that he was easily distracted by delusions and hallucinations and his perception and judgment were grossly disorganized. He had periodic episodes of assaultiveness and hyperactivity. In between these episodes he was completely out of contact, seclusive and inaccessible for any form of therapy.

On Nov. 28, 1949, 3 cc. of 2 per cent novocain were injected into both frontal lobes very slowly. The patient answered questions during the entire procedure. He appeared to have some chills during the injection but they were not suggestive of

convulsions. He was watched carefully for 2 hours during which he seemed to be in a slightly better contact, but otherwise was not greatly improved. About 4 hours after injection, there suddenly developed a series of alarming convulsions and he went into deep coma with circulatory and respiratory collapse. He was treated with a lumbar puncture and supportive measures. After 12 hours, his condition gradually improved and he returned to the preoperative state.

On Dec. 12, 1949, a bilateral lobotomy was performed. Following the operation, the patient showed no marked change in his behavior. Re-evaluation 6 months after lobotomy showed that he had lost some spontaneity and appeared more depressed. He spoke only in a low voice. He was again seclusive and had no contact with other patients. He was irritable and often assaultive. Now, 18 months after lobotomy, he is still classified as a poor result.

SUMMARY. *A catatonic schizophreniac who showed no improvement under insulin and shock treatment. Novocainization produced no marked change in his behavior. The observations were complicated by the fact that he had an alarming vasomotor collapse and became comatose about 4 hours after the injection. A lobotomy has not produced improvement in his behavior or mental state up to 6 months.*

Case 12. No. 3993. S.O'N., a 33-year-old man, had symptoms of schizophrenia since 1943. Since hospitalization, his behavior has been one of constant hyperactivity with delusions and hallucinations. He has been residing in the semi-disturbed ward since 1946. His conversation is usually disconnected and irrelevant. He states that something was wrong with his blood and that his body was a physical wreck. He kept on hearing voices through the walls. He often smiled and laughed in a silly and inappropriate manner. He needed constant sedation. He was a severe management problem.

Novocainization was done on two occasions, Jan. 9 and Jan. 12, 1950. Three cc. of 2 per cent novocain were injected into each frontal lobe. A record was made of his conversation and reaction during and after the injection. He showed practically no change in his speech or behavior, continuing to be obscene, overtalkative and overproductive, constantly reacting to active delusions and hallucinations.

On Jan. 16, 1950, a bilateral prefrontal lobotomy was performed. There was practically no change in his behavior. He continued to be hyperactive and violent. Postoperative X-rays of the skull showed that the level of the lobotomy was much more anterior than the routine cuts that we had been doing here. Because of his continuing bad behavior, it was felt that the lobotomy should be revised.

On Feb. 17, 1950, a slightly more posterior prefrontal lobotomy was performed bilaterally. After the second operation, the patient showed a definite improvement for about 4 weeks after which he relapsed into his preoperative state of constant hyperactivity. At present, 16 months after the second lobotomy, the result is still poor.

SUMMARY. *A hyperactive deteriorated hebephrenic schizophreniac. Novocainization produced no change. Two successive lobotomies gave no improvement.*

Case. 13. No. 4879. W.H., a 30-year-old man, has had symptoms of mental disease since 1946. He had many delusional ideas and has had homicidal tendencies. Electroshock therapy several times gave temporary improvement. Re-evaluation late in 1949 showed that at times he was calm and well adjusted, with periods when he became tense and negativistic, resistive and hyperactive, teasing and irritative to other patients. Then he had to be placed in neutral wet packs. Often he had crying spells and expressed the desire to die.

Novocainizations were done on two occasions, Jan. 2 and Jan. 18, 1950. Each

of these injections was done when he showed signs of emotional tension and appeared about "to blow up." A wild stare in his eyes was noted at such times. After the first injection, he became less tense. After the second novocainization he laughed hilariously and inappropriately and kept on tapping on the table with his fingers. His mother interpreted this tapping of the fingers as a recall to the days when he used to work as a telegraph operator. This mood of elation and overproductivity lasted for about 3 hours after each injection, when he became tense and seclusive again.

A bilateral prefrontal lobotomy was done on Jan. 20, 1950. During the first 2 months after operation he was again hyperactive. His ideas were flighty and very similar to his reactions after his second novocainization. In the 3rd postoperative month, however, he showed a definite improvement, which then became more and more encouraging. Approximately 5 months after operation re-evaluation showed that he denied any hallucinations and delusions but admitted that he had had them before the operation. His conversation was relevant and coherent but slightly underproductive. He carried on work in the manual-arts shop and did work in the radio shop.

He returned home the next month, operated a small radio repair shop of his own and was discharged from the hospital 18 months after lobotomy.

SUMMARY. *A young catatonic schizophreniac who showed slight improvement after electroshock therapy but still had periods of hyperactivity and deep emotional tension. Novocainization on two occasions produced favorable results on behavior. The results from lobotomy were excellent, and he was discharged 18 months after lobotomy.*

Case 14. No. 3378 C.V.A. N.W., a 30-year-old man, had symptoms of a psychosis in 1944 which was characterized by excitement, confusion, misinterpretation, auditory hallucinations, homosexual ideas of reference and grandiose delusions. Electric shock treatments were given in 1944 with temporary improvement. He was found to have a mild diabetes which could be controlled with insulin and diet. On the ward he had been seclusive, preoccupied, mumbling to himself in response to hallucinations, and stated that Governor Dewey and President Truman were his sons and that he had many wives and many children. At times he would come into better contacts with reality, and would be pleasant and friendly.

Novocainizations were done on two occasions, on Jan. 31, and Feb. 2, 1950. An EEG was done at the same time that the injections were made. The first EEG showed no changes. The second EEG showed a random 6–7/sec. wave in the left frontal region. He continued to have hallucinations and it was impossible to get any satisfactory psychological responses from him after the novocainizations.

On Feb. 6, 1950, a bilateral lobotomy was performed. During the operation it was noted that the arachnoid membrane was greatly thickened bilaterally. A biopsy was taken. Aside from the thickened arachnoid and some disorganization of the cortical patterns nothing else characteristic was found.

After the lobotomy, the patient showed practically no improvement. He displayed homosexual tendencies almost immediately. He soiled and wet himself frequently. He became hyperactive and violent at times and had to be placed in packs. He continued to have delusions and thought that one of the nurses was Norma Shearer. He slapped other patients and needed sedations frequently.

SUMMARY. *A 30-year-old man with paranoid schizophrenia and mild diabetes. Novocainization on two occasions showed no changes in his EEG or in his behavior patterns, and did not eliminate his hallucinations. Lobotomy also has produced little improvement up to 17 months.*

Case 15. No. 4924 C.V.A. H.A., a 25-year-old man, was manifestly psychotic for at least 3 years prior to admission, exhibiting hyperactivities and reacting to delusional concepts. He said that "his soul had left his body via his eyes in 1945." In February 1947, a series of electroshock treatments was administered with slight improvement which was unsustained. A second series of electroshock was started in March and ended in May 1947. Psychological tests done in 1948 indicated an average to a possibly superior intellectual capacity. In January 1949 the patient became hyperactive and assaulted other patients. The hyperactive and assaultive periods lasted 2 to 6 weeks. The prodromal symptom of this hyperactive episode consisted of his jumping up and clicking his heels together. Sedative hydrotherapy was required during his hyperactive periods. During his "good" intervals, he was seclusive, asocial, preoccupied, idle and required supervision at meals.

On Jan. 27, 1945, both frontal lobes were injected with 2 per cent novocain. An EEG record was taken at the time of injection. This showed some random slow waves in both frontal regions which had not been present in his preoperative record. Subjectively, the patient felt better and he told his brother that "he had gotten rid of some of the dirt which he acquired in Europe." The injection was done during one of his "good" periods so it was impossible to tell whether the novocainization had changed his behavior for the better.

A second novocainization was done on Feb. 9, 1950; 3 cc. of 2 per cent novocain were injected into the right frontal lobe only. There was no marked clinical change.

A third novocainization was done on Feb. 20, 1950; $2\frac{1}{2}$ cc. of 2 per cent novocain were injected into the left frontal lobe. No matter which side of the frontal lobe was injected, random slow waves appeared over the injected side first and spread over to the other lobe within $\frac{1}{2}$ hour of the injection. Again the patient subjectively felt more relaxed and claimed benefit from the injections. Objectively, there was no change in his general behavior that could be attributed to the injection.

On Feb. 21, 1950, bilateral prefrontal lobotomy was performed. During the 3 months after operation, his behavior improved. He became more spontaneous and more cooperative. There was no bed wetting and he had no seizures. He was doing well on the "push" program. Towards the middle of the 4th month, however, he became depressed and confused, climbed over the hospital fence and tried to escape. Re-evaluation was classified as no improvement up to 17 months.

SUMMARY. *Catatonic type of schizophrenia of 3 years' duration. Novocainization did not give any clear-cut improvement. Lobotomy caused temporary improvement for 3 months with relapse into mental confusion and depression in the 4th month.*

Case 16. No. 4967 C.V.A. S.A., a 25-year-old man, has had symptoms of mental illness since 1947 when he became violent in church and said that the devil was talking to the priest. He threatened to kill his mother and did not recognize his brother. He received electroshock treatment in 1947 without improvement. He has been on a semi-disturbed ward during the last 2 years and has remained confused, hyperactive, asocial, indifferent and idle. He often was surly, irritable and assaultive. Treatment with hydrotherapy and medical rehabilitation gave no improvement. Psychological examination was not satisfactory because he was so disorganized and incoherent.

On March 7, 1950, 3 cc. of 2 per cent novocain were injected into each frontal lobe. At that time the patient was actively hallucinating and talking incoherently. A sound record was made of his conversation. Immediately after the novocainization,

the patient became more rational, was in much better contact, and could answer some questions coherently. This favorable reaction lasted for about 1½ hours. Then he became obscene again and talked in an incoherent fashion, as before.

On March 13, 1950, bilateral prefrontal lobotomy was performed with the McKenzie leucotome. Improvement was noticed almost immediately after operation. Nine months later, he was sent home on trial visit and he has been making satisfactory adjustment up to 15 months.

SUMMARY. *A catatonic schizophreniac with symptoms of approximately 3 years' duration. One novocainization produced a marked improvement in his hyperactive behavior. At the present time, 15 months after lobotomy, the results have been also very encouraging.*

Case 17. No. 1531 C.V.A. P.J., a 58-year-old man, has had signs of mental illness for at least 12 years. He received 44 electroshock treatments in 1948 without improvement. He continued to be threatening, belligerent and assaultive. Psychological examination showed the patient to be confused and incoherent. He could not express himself in English completely, using the French-Canadian tongue most of the time. The tests showed that "he had poor contacts with reality and was absorbed into an autistic world of his own with a schizophrenic flavor." Because of his hyperactive and antagonistic behavior, he had been a major management problem in this hospital.

On March 15, 1950, 3 cc. of 2 per cent novocain were injected into the frontal lobes. The patient had been very antagonistic to nurses and suspicious just before the injection. After the novocainization, he became much quieter, was able to talk to the doctor, was not tense, and was much more cooperative. He allowed the nurses to take his blood pressure every half hour without complaint. This favorable behavior, however, lasted only about 4 hours, when he reverted to his antagonistic and suspicious attitude.

On March 23, 1950, a bilateral lobotomy was performed with the McKenzie leucotome. He showed little change in his behavior during the 1st month after operation. By the 3rd month the ward attendants and nurses noted much improvement in his behavior. They were able to "train him better." They stated that he became now "more like a human being." Previously, he had refused food many times but now he has been eating well. He soiled and wet himself at first following operation, but this soon cleared up. He mutters a great deal to himself. He has had no seizures. At present, 15 months after operation, he is still in the hospital but is no longer a management problem and is classified as showing moderate improvement.

SUMMARY. *A 58-year-old French-Canadian with a history of mental illness for 12 years. Novocainization gave a favorable result which lasted about 4 hours. Results after lobotomy have been favorable up to 15 months.*

Case 18. No. 2675 C.V.A. M.M., a 34-year-old man, has had symptoms of catatonic schizophrenic reaction since induction into the Army in 1942. He received 3 series of electroshock treatment without benefit. During the last few months before lobotomy the patient had been negativistic, mute, and inactive. At other times he would make sudden assaults on the personnel both on the ward and in the occupational therapy shop. Psychological tests were not satisfactory.

On May 11, 1950, 3 cc. of 2 per cent novocain were injected into each frontal lobe through drill holes which had been made 3 days previously. The patient was mute before the injection and he remained mute after the injection. He had been

having some seizures before the injection, possibly as a result of the repeated electroshock treatments. He had no adverse reaction after the injection. However, there was no improvement in his general behavior as a result of the novocainization.

On May 17, 1950, a bilateral lobotomy was done with a McKenzie leucotome. At the present time, about 13 months after operation, he has shown no marked changes in his behavior. He remains mute and catatonic and shows signs of further deterioration.

SUMMARY. *Catatonic schizophrenia of 8 years' duration, with no response to electric shock treatments. Novocainization failed to bring any change in his mutism and catatonic withdrawal. Lobotomy has not changed his psychosis or behavior up to 13 months.*

Case 19. No. 4193 C.V.A. J.S., a 24-year-old man, has had symptoms of mental illness for 4 years. He attempted to commit suicide by stabbing himself in the throat. This was the first symptom of his mental illness. A diagnosis of catatonic schizophrenia was made, and he received a series of electroshock treatments in 1946 without any improvement. Just before the present treatment he had been delusional, destructive, belligerent, vulgar and obscene. There are many reports of assaults committed by the patient on the personnel during the last 3 to 4 years. He was constantly in camisole or packs. He was always dirty and his fingers were always burned from cigarettes.

Novocainization of the frontal lobes with 3 cc. of 2 per cent novocain was done on two occasions, May 15 and May 19, 1950. Both of the injections were done during a period when he was obscene, vulgar, and threatening to the personnel. He refused to cooperate and it required four attendants to put him on a stretcher to go to the operating room. After each injection, however, he became more cooperative. He was still overtalkative with incoherent speech most of the time but he appeared to be in better contact. Before the injection, when we asked his name, he gave irrelevant answers. After the injection he at least answered once with his full name to a similar question. He allowed the personnel to take his temperature and to take his blood pressure. This had been practically impossible before the novocainization. These favorable reactions lasted only about 4 to 6 hours.

A lobotomy was performed on May 24, 1950. Improvement was slow and gradual. His psychosis did not show much change, but his need for sedation gradually decreased. By 13 months after operation, he was allowed to go home on weekends.

SUMMARY. *Catatonic schizophrenia of 4 years' duration, characterized by destructive and belligerent behavior, obscene speech and poor contact. Novocainization on two occasions produced encouraging responses from the patient. Result of lobotomy has also been encouraging up to 13 months.*

Case 20. No. 4624 C.V.A. R.M. was a 37-year-old man who spoke nothing but Italian although it was clear that he understood some English. He has had signs of severe mental illness since 1944. He felt that he was being held a prisoner by a foreign army and that some one was influencing his mind and was using machinery to act on his brain. At the last mental examination, it was noted that the patient understood very little English and that his conversation in Italian was totally irrelevant, incoherent and incomprehensible. On the ward, he had been excited, noisy and hyperactive at intervals. He even threw furniture about and scolded other patients. At times, he would stand up and shake himself like a dog and apparently scolded imaginary people violently. He required sedation and hydrotherapy frequently.

On May 26, 1950, novocainization was performed using 3 cc. of 2 per cent novo-

cain. This was immediately after one of his hyperactive episodes. After the injection he quieted down and behaved well on the ward for about 4 to 6 hours.

During the second injection on June 1, 1950, an interpreter was available. Before the injection, the patient would not talk and would not answer any questions asked by the interpreter. Within 5 minutes after injection, the patient was talking coherently and intelligently so that we could obtain a 15-minute interview with him. He denied that he had any delusions or hallucinations. However, he stated: "I'm not so dumb as you think I am. I know what is going on. I am as good as anybody else." Another interesting item was brought out by the novocainization interview. Previously, no one had been able to obtain any history of somatic complaints. During this interview, however, the patient complained that he had pain in the epigastrium, coming on soon after each meal. Then it was noted by the attendants that his hyperactive episodes occurred mostly, although not always, about 10 to 15 minutes after each meal. After these two novocainizations, it was noted that the patient's attitude toward the attendants and staff was much more cheerful and cooperative than before. A GI series showed a hiatus hernia involving the upper end of the stomach.

A prefrontal lobotomy was performed on June 8, 1950. The patient behaved much better for 3 months after operation. He then became seclusive and regressive up to 12 months.

SUMMARY. *A catatonic schizophrenia of 6 years' duration. Behavior characterized by mutism and withdrawal, with periods of assaultiveness and hyperactivity. Novocainization on two occasions interrupted the catatonic withdrawal so that the patient came into better contact with his surroundings. Twelve months after lobotomy, however, re-examination failed to show any substantial improvement.*

PROCAINE BLOCK OF FRONTAL WHITE FIBERS IN 6 NONPSYCHOTIC PATIENTS

Case 21. No. 32870 S.M.H. E.H., a single woman aged 49, had been seen by a great many physicians for 20 years, or more, because of a legion of complaints referable to all systems of the body. Most of her complaints centered about the lower bowel and bladder. No abnormal findings of note were ever noted. The impression was that of a very severe psychoneurosis. In 1945, she began to show signs of a degenerative disease of the nervous system that has progressed up to date and has been diagnosed as multiple sclerosis. Whether this is correctly named or not is immaterial. There are abnormal signs referable to the cerebellum, pyramidal tracts, optic nerves, etc. About this time, 1945, she began to be paranoid, obstinate, suspicious, profane and obscene. She entered upon a parade from one institution to another, never staying more than a few weeks in any one place. Her greatest obsession was that of foreign bodies in the rectum or genital tract that required repeated enemata for removal.

On May 3, 1949, burr holes were made over each frontal area. On May 6, 6 cc. of 1 per cent procaine were injected into each frontal lobe. A rather dramatic change was noted in her behavior. She was no longer suspicious of being poisoned, did not complain of her lower bowel or bladder, and was not profane. This effect lasted about 6 hours.

On May 7, the injection was repeated. Again a desirable effect was noted for a short time.

On May 9, another injection was made, using saline instead of procaine. A short beneficial effect was noted.

On May 14, a needle was inserted but nothing was injected. No effect was noted.

On May 16, a left prefrontal lobotomy was done. A moderate improvement in behavior resulted.

On June 1, the right prefrontal fibers were cut. She was last seen June 1950. She is able to be cared for without special nurses. She is no longer disturbed, profane, suspicious of poison and has lost many of her obsessions. Her physicians think she is much improved.

SUMMARY. *It is felt by impartial observers that the novocain block gave an accurate prediction of the effect of prefrontal lobotomy in this obsessive schizophrenic patient.*

Case 22. No. 110055 S.M.H. E.B., a 59-year-old male, was first seen in April 1949, with complaints of a hypochondriacal nature that would actually consume an hour to relate. He dates the onset of his difficulties to a minor accident while serving in the first World War. He has married twice and had one child by his first wife in 1919. He has done a little work as a chicken farmer, but for 20 years has lived mainly through his wife's efforts and a Veteran's pension. His life has been devoted to his complaints and futile efforts to obtain relief from them.

His most constant complaint is headache for which he has had innumerable things done to his nose and throat, teeth, scalp and its arteries. His next most consistent complaint is referable to his joints, knees and hips in particular. Heart and lung complaints are numerous. Over a period of years he has been hypersexed but lately has been impotent most of the time. He had become seclusive and did not want to leave the house. At times he is abusive and threatening to relatives but he has never actually assaulted any one.

Physical examination showed little of note. In general he was considered normal.

On April 15, 1949, 4 cc. of 1 per cent procaine were injected into each frontal lobe. For 18 to 24 hours he said he "felt fine." Gradually he reverted to voicing his former complaints.

A second injection was done on April 20, using 6 cc. on each side. The result was the same as that noted following the first injection but more profound. He was discharged for 2 months to note the effect. Both the patient and his wife felt that he had been temporarily improved to a point where they would favor making the result permanent if possible.

On June 27, 1949, a bilateral frontal lobotomy was performed without incident. Up to the time of death, June, 1950, from a coronary infarction, he was without complaint unless he was questioned. He remained amenable to going out for mild recreation at the movies, and bingo games. He did a small amount of useful work. His family was much satisfied with the result obtained even though he could not return to an earning capacity.

Case 23. No. 294983 S.M.H. M.H. was a 72-year-old widow, with the chief complaints of headache and crying spells. She was the mother of twelve children and had been considered to be in good health until about 2 years prior to entry. Shortly before this her husband had died, and since then she had made her home with various sons and daughters. The husband and wife had had a long marriage and had been very dependent upon each other: "We were a couple of old posts holding each other up."

The headache was described as throbbing, steady, generalized, and more marked in the supraorbital area than elsewhere. Sometimes she became slightly nauseated but did not vomit. She was much depressed at times, and had rather frequent crying spells. She had given up practically all types of work; and had no particular means of self-amusement. While she is an intelligent individual, she had never had an opportunity to go to school and actually could not read or write more than to sign a name. She did not care to go to the movies or listen to a radio. She ate sparingly and had to be urged. She had rubbed the skin of the forehead to a point where it was almost paper-thin.

She was a small, slight, elderly, white-haired woman who appeared tense during examination. She was constantly fidgeting with her hands or rubbing her forehead. She had lost some weight because of lack of interest in food.

The physical findings were normal aside from evidence of age and a generalized arteriosclerosis.

X-rays of the skull were within normal limits. Blood, urine and stools were normal. Blood Wassermann was negative. CSF, studied at another hospital, was normal.

The impression was that we were dealing with an involutional type of melancholia secondary to cerebral arteriosclerosis.

On April 15, 1949, under novocain anesthesia, a burr hole was made in the mid portion of each frontal bone below the hair line. Three cc. of 1 per cent novocain with a few drops of adrenalin to the ounce were used to infiltrate the white fibers of the frontal pole. Following this procedure the patient and her relatives felt that she was improved as far as her complaint of headache was concerned. She did complain of the soreness of the wound. She did not ask for medication although she had been in the habit of taking a good deal of medication while at home.

On April 19, 1949, the procedure was repeated, using 5 cc. A very definite improvement resulted. For the first time in months she conversed with relatives without dwelling almost constantly on the subject of headache. She was sent home to think over the matter of a lobotomy. After about 2 months, she and her family decided that the postinjectional state was a desired one.

On July 8, 1949, a bilateral prefrontal lobotomy was carried out without incident. Up to date she has had a marked relief of her subjective complaints. She does a little housework, enjoys going for auto rides, etc. Her family feel that the result has been a desired one.

It is felt that the final result was predicted rather accurately by novocain block.

Following is an excerpt from a letter of the daughter of M.H. dated Aug. 23, 1949, which is about $1\frac{1}{2}$ months after operation:

"The headache is gone. Sometimes when Mom is provoked with one of us, she says she has one. Mom looks much improved, eats much better, has gained a little. We really think it is wonderful how she came through the operation. It is a pleasure to see her eat her meals and see her without that head pain." This same state has persisted.

Case 24. No. 285183 S.M.H. D.S. was a 38-year-old woman whose main complaints centered about the head and neck. Her complaints were legion, such as a feeling of snapping in the left upper jaw, constant headache, asymmetry of the face, pain in the back of the neck, inability to sleep, feelings of floating in the air, feelings of depression, pain beneath the left breast, feeling of constriction of the hands. There

TABLE 1

Summary of novocainization in 20 schizophrenic patients

	Diagnosis	Immediate Effects of Novocainization on Behavior	Period of Observation (Months)	Effect of Lobotomy on Psychosis	Value of Lobotomy in Management of Patient
Correct Predictions—11 cases					
1. Case 2, F.B.	Paranoid	Improved	24	Greatly improved	Excellent—discharged—employed full time
2. Case 6, H.L.	Hebephrenic	Improved	18	Greatly improved	Excellent—at home on trial visit
3. Case 8, S.R.	Catatonic	Improved	20	Moderately improved	Excellent—no longer disturbed
4. Case 10, T.S.	Catatonic	Improved	21	Moderately improved	Excellent—at home on trial visit
5. Case 13, W.H.	Hebephrenic	Improved	17	Greatly improved	Excellent—discharged—employed part time
6. Case 16, S.A.	Hebephrenic	Improved	15	Moderately improved	Excellent—at home on trial visit
7. Case 17, P.J.	Paranoid	Improved	15	Slightly improved	Good—no longer disturbed
8. Case 19, J.S.	Hebephrenic	Improved	13	Slightly improved	Good—goes home on week-ends
9. Case 1, L. S.	Hebephrenic	Not improved	24	No improvement	Poor—still frequently disturbed
10. Case 5, A.F.	Hebephrenic	Not improved	22	No improvement	Poor—still occasionally disturbed
11. Case 12, S.O.	Hebephrenic	Not improved	16	No improvement	Poor—frequently disturbed
Wrong Predictions—3 cases					
12. Case 4, H.C.	Catatonic	Improved	23	No improvement	Poor—frequently disturbed
13. Case 7, J.C.	Paranoid	Improved	6	No improvement	Poor—committed suicide at home
14. Case 20, R.M.	Catatonic	Improved	12	No improvement	Poor—frequently disturbed
Questionable Results—6 cases					
15. Case 3, S.B.	Catatonic	No change; remained mute and withdrawn	24	No improvement	Fair—easier to manage—but totally unproductive
16. Case 9, E.S.	Catatonic	No change; remained mute and withdrawn	19	No improvement	Fair—easier to manage—but totally unproductive
17. Case 11, W.L.	Catatonic	No change; remained mute and withdrawn	18	No improvement	Fair—easier to manage—but totally unproductive
18. Case 14, N.W.	Paranoid	No perceptible changes in responses	17	No improvement	Good—no longer disturbed
19. Case 15, H.A.	Catatonic	No perceptible changes in responses	17	No improvement	Fair—no longer disturbed but would become confused
20. Case 18, M.M.	Catatonic	No perceptible changes in responses	13	No improvement	Poor—requires sedation frequently

was no end to the list of symptoms if they were brought to her attention in any way.

She was an only child of a moonshiner in a southern mountain community. She was married at the age of 14, and had her first child at 15. She was divorced at 18 when pregnant. An abortion was induced and an infection resulted. Both Fallopian tubes were removed. She married again and lived with her husband for 5 years. In 1941 she was in an auto accident, after which she was unconscious for 3 days and hospitalized for 4 months. In 1943 she was married again. In 1944 she was knocked "down, but not out" by her husband, and was divorced. In 1946 she was unconscious

all one night after a fall while drunk. In 1947 she had all her teeth out because of headache. She was very depressed in 1947 when her "boy friend" committed suicide by slashing wrists, cutting throat, setting bed on fire, and finally jumping out of window.

The patient claimed to be working as a waitress and caretaker in an apartment house. She had tried various means to cure herself of alcoholism and drugs because of the gastritis that follows overindulgence. "The trouble with Alcoholics Anonymous is that they provided me with male companions who didn't keep their minds on alcohol."

So far as could be learned, she had never been disoriented for a period longer than required for sobering up. She stated that she had not been hallucinative. She had never been suicidal. She did not appear deteriorated to any particular extent. On the other hand, she had never been at a height where she could deteriorate very far.

She was a tall, slight, slender, very active individual. She took fastidious care of her hair, skin and nails, and altogether presented a rather good appearance.

The first prefrontal novocain injection was done on April 20, 1949. Following the procedure, she seemed quieter, a little less garrulous and stated that for the first time in months she was able to sleep both during the day and at night with a little or no medication.

The procedure was repeated 6 days later—again with a marked beneficial effect on her volume and content of complaints. After several days' observation, she wanted to go home because she "had certain housekeeping matters to take care of." She was seen 2 months later and, according to her, she was sleeping well. She had gained 15 to 20 lbs. in weight and was not taking any drugs.

A prefrontal lobotomy was not done inasmuch as a desired effect was obtained without it. The patient was seen 6 months later in the emergency ward because of extreme acute alcoholism. After the effects of this were over her stream of conversation appeared normal for her. Again, it was not felt that a lobotomy was indicated.

SUMMARY. *A patient with complaints of an extreme hypochondriacal nature. Two frontal lobe injections were carried out. Because of, or in spite of, the procedures carried out, there was a temporary alteration in the nature and volume of her subjective complaints. Tendency toward alcoholism is unchanged.*

Case 25. No. 245593 S.M.H. P.E., a 52-year-old woman, constantly complained of pain in the left side of the face. She had been observed in the clinic for over 4 years because of various organic disorders, such as coronary occlusion, old; nontoxic goiter; strangulated ventral hernia; hypertensive cardiovascular disease; and numerous minor complaints.

In the latter part of 1949, a left upper molar tooth was extracted. Two months later, she began to complain of a diffuse left-sided facial pain which was described as burning in character. Some temporary relief was obtained from cocainization of the left sphenopalatine ganglion, and also from a left stellate ganglion block. The pain never appeared typical of a trigeminal neuralgia. She had become nearly addicted to drugs.

On Aug. 22, 1949, bilateral frontal burr holes were made. The pia arachnoid was sealed to the underlying cortex by means of the endotherm. Novocain was not injected. The patient had temporary relief from her complaints and was discharged. In January 1950, she returned with her previous complaints and with signs of coronary insufficiency.

On Jan. 27, 1950, 3 cc. of 2 per cent procaine were injected very slowly into each frontal lobe. Within a period of 10 minutes she stated that pain had disappeared together with tenderness and soreness of the skin of the left side of the face.

On April 27, 1950, 3 cc. of 2 per cent procaine were injected into the left frontal lobe, with relief of her complaints for several days.

On May 3, 1950, the injection was repeated in the left frontal lobe. Again, the patient stated that she had complete relief from her pain, until the date of discharge, May 11, 1950.

The patient will be observed further to note the effect of the novocain injection before considering prefrontal lobotomy.

SUMMARY. *A 52-year-old woman complaining of left facial pain of an atypical nature obtained relief in a matter of hours to days following novocain block of the white fibers of one or both frontal lobes.*

Case 26. No. 306170 S.M.H. E.P. complained mainly of intolerable itching sensation of the right side of the face and of the right eyeball.

In April 1949 she had had a mild attack of herpes zoster involving the right supraorbital region. Secondary infection of the skin was treated with aureomycin with good effect. Shortly after the infection cleared up she began to complain of an intolerable itching sensation limited to the right side of the forehead, right eyeball, and occasionally the left eyeball. The complaint was not a usual one for a postherpetic neuralgia. It had not responded to extensive and excessive medication. She had complained of migraine headaches for many years.

She was a fairly well preserved elderly woman, constantly rubbing her forehead with her hand. She appeared tense, moderately depressed and anxious. It was noted that her complaints disappeared almost entirely when a favorite son was present and sitting by the bedside. In the presence of certain other relatives, there was an adverse effect upon her complaints.

On Feb. 8, 1950, bilateral frontal burr holes were made.

On Feb. 20, 1950, 3 cc. of 2 per cent novocain were injected into each frontal lobe. There was no beneficial effect noted following this procedure.

A prefrontal lobotomy was not carried out because of the failure to obtain a desired effect and because the complaints were not typical of postherpetic neuralgia. It was felt that a complaint was being used to dominate a social situation.

SUMMARY

Procaine injections into the white fibers of the frontal lobes of the brain may be used to aid in prognosticating the effect of a prefrontal lobotomy upon the behavior of psychotic patients. It will not aid in predicting the final course of the psychosis. This procedure is most useful in predicting relief from unusual complaints of pain by a prefrontal lobotomy.

Novocainization is most reliable when done in psychotic patients during their period of overactivity.

The observed effects upon behavior following novocainization follow the effects of lobotomy in 2 out of 3 cases.

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RECOVERY FROM THE DECEREBRATE STATE ASSOCIATED WITH SUPRATENTORIAL SPACE-TAKING LESIONS

HOWARD FREEDMAN, M.D.

State University of New York Medical Center, Department of Surgery, New York, and Neurosurgical Service, Kings County Hospital, Brooklyn, New York

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EXTENSOR rigidity occurring in the course of various intracranial diseases has been described in many publications. The level of impaired neurological function responsible for the appearance of this phenomenon was demonstrated by the classical experiments of Sherrington[22] and his co-workers, whose "decerebrate" animals duplicated almost exactly the extensor rigidity seen in man. Anatomical studies of some patients who prior to death displayed the features of "decerebrate rigidity" have revealed hemorrhages in the upper brain stem.

It was recognized early that the exhibition of the decerebrate attitude was of grave prognostic import, especially when it came in the course of supratentorial space-taking lesions—hemorrhage, abscess, or tumor. In fact, it has been and unfortunately continues to be, the opinion of many neurologists and some neurosurgeons in particular that the supervention of the decerebrate attitude mitigates against if not actually precludes the possibility of recovery regardless of therapy. It is the purpose of this report to present evidence indicating that prompt definitive surgery may be followed by survival and, in many instances, by complete recovery.

For the purpose of this discussion, the decerebrate attitude may be described as essentially one of extensor rigidity; the head is retracted, upper extremities are adducted and internally rotated, forearms extended and hyperpronated, and hands flexed. The fingers are usually flexed at the metacarpophalangeal joints but extended and adducted distally. Variations of the posture are observed, including flexion of forearm or alternation between the extended and the flexed positions. In that case, extension usually returns following strong mechanical stimulus. The lower extremities have always been found to be extended, adducted and internally rotated. The large toes may be rigid in the "chronic Babinski" position following stimulus. The tonic neck reflexes of Magnus and DeKleijn have been reported but we have not observed their presence in this series.

Usually, alterations in the vital functions occur concomitantly with the appearance of the abnormalities of muscle tone: the pulse gradually increases in rapidity, respirations usually become rapid and blowing and are frequently characterized by irregular periods of apnea. The blood pres-

sure may be elevated and the body temperature frequently rises precipitously if unchecked.

Abnormalities of pupillary function with respect to size and reactivity to light, and paresis of one or more of the extraocular muscles not infrequently accompany the decerebrate attitude.

During the past 20 years, a large number of patients manifesting this clinical phenomenon have been observed. The 19 patients selected for this report were studied on the Neurosurgical Service of Dr. Jefferson Browder at the Kings County Hospital, Brooklyn, New York over a period of 3 years (1947–1950) and all were personally observed by the author. In all instances supratentorial lesions were present and recovery followed appropriate surgical therapy.

In 14 cases bilateral extensor rigidity was present and in the remainder there was involvement of one or both extremities on one side. The underlying conditions included 12 subdural hematomas, 2 temporal lobe tumors, 1 frontal lobe abscess, 3 epidural hematomas, and 1 instance of dissolution of a temporal lobe following contact trauma of the head. In each case, operative treatment consisted of evacuation of the mass.

The duration of the decerebrate state before operation varied from less than 1 hour in 7 cases to as long as 20 hours in 2 instances. In 2 cases, the patients were admitted to the hospital in the decerebrate state with external evidence of contact trauma of the head but additional histories could not be obtained. In most cases, improvement following surgery was continuous but in 2 instances, evidence of rigidity reappeared after varying intervals and again disappeared following further appropriate surgical measures.

In only 3 cases were the pupils thought to be normal in size and in their response to light. They were widely dilated, equal and without reaction to light in 7 cases, unequal and fixed to light in 5, unequal with the dilated pupil fixed to light in 2, and unequal but reactive to light in 1. In no instance were the pupils "pinpoint." In 1 case the state of the pupils was not recorded. In those instances wherein the pupils were unequal, the larger was ipsilateral to the intracranial lesion in 6 instances and on the opposite side in 1. In the eighth case the lesion was a huge bilateral frontal epidural hematoma.

Increased intracranial tension as evidenced by papilledema was observed in only 7 cases but that is not remarkable because most of the symptoms were of relatively short duration. It has been our policy not to disturb the cerebrospinal fluid dynamics where there is clinical evidence of dysfunction of midbrain structures and for that reason the cerebrospinal fluid pressure was measured in only 6 cases. In 4 of these the pressure was between 240 and 340 mm. water and in the other 2 it was 100 mm. water or less.

The degree of recovery varied between absence of any residual to severe and incapacitating defects requiring continued institutional confinement. Of those individuals having no demonstrable residual neurological disturb-

ances, 3 had had extensor rigidity bilaterally and 2 had had unilateral involvement. The 2 patients with tumors recovered with no residual other than that resulting from the neoplasms and should be classed an excellent result. Mild residua, such as paresis of one or more extremities or persistent extraocular muscle dysfunction that did not interfere with rehabilitation, were present in 5 of those patients who had had bilateral rigidity and in 1 in whom the rigidity had been unilateral. One patient in this group had a residual of homonymous hemianopsia. The remaining 6 patients had such severe disturbances in motor function or intellectual capacity that rehabilitation was not possible or continual institutional confinement was required. Thus it may be considered that in 13 of the 19 patients of this series the outcome was reasonably satisfactory. It is of interest to note that there was no correlation between the duration of the decerebrate attitude prior to operation and the eventual outcome, and that both of the patients who had repeated periods of decerebration made satisfactory recoveries.

DISCUSSION

The presence of hemorrhages in the brain stem associated with supratentorial hemorrhage was reported in the pathological studies of Attwater[3] and Greenacre[10] before their clinical significance was appreciated. Shortly after the publication of Sherrington's observations on the decerebrate state in animals, Wilson[29] called attention to the parallel between the attitude seen in those animals and that accompanying certain diseases in man. In 1921, Jefferson[11] reported 2 cases of epidural hematomas wherein bilateral extensor rigidity was observed prior to death. No gross alterations in the brain stems were found, and the conclusion was drawn that *physiological* interruption of brain-stem pathways had resulted from alteration in the circulation to their area. With this conclusion we are in agreement. Additional articles[6,26,27,28] describing the decerebrate attitude in man appeared, and the presence of hemorrhage in the brain stem was demonstrated only in some of the cases.

There was much speculation as to the cause of the alteration in blood supply to the brain stem associated with supratentorial lesions. Adolf Meyer[14] had called attention to the fact that supratentorial tumors were frequently associated with herniation of portions of the brain under the falx and through the tentorial incisura. He suggested[15] the possibility that these herniations might play a part in the disturbed function of the brain stem. Vincent, David, and Thiébaut[25] correlated the presence of herniation of the medial aspect of the temporal lobe through the incisura tentorii associated with supratentorial tumors, and the alterations in the brain stem formulating the syndrome of the early and late effects of this phenomenon. They also called attention to the fact that the removal of cerebrospinal fluid via the lumbar route may increase the degree of herniation and result in further damage to the midbrain structures. Since then, numerous contributions[1,2,5,8,12,16,19–21,24] of both clinical and pathological natures have con-

firmed their observations. It now seems fairly well established that herniation of the medial aspect of the temporal lobe through the incisura tentorii (the so-called "temporal pressure cone") can produce alterations of the blood supply to the brain stem and result in the appearance of the decerebrate attitude.

The temporal pressure cone and its attendant features have been produced experimentally[19] by increasing the intracranial tension with the aid of artificial masses in the epidural or subdural spaces over the cerebral hemispheres. The decerebrate state so produced was reversible if the pressure was relieved promptly. Some observers have expressed the opinion that a similar situation might occur in man. However, surgeons have hitherto seemed reluctant to undertake operative measures in the presence of decerebrate rigidity. We have been able to find only three previous reports in the literature in which there is mentioned the recovery of patients in whom extensor rigidity developed in the course of supratentorial space-taking lesions. Reid[19] mentioned a patient who, after the introduction of air into the ventricles, became rigid, stopped breathing and had a fixed dilated pupil. Rapid recovery ensued after releasing the intraventricular pressure. Gallagher and Browder,[9] in a review of a series of 100 cases of epidural hemorrhages, reported the presence of extensor rigidity in 38 of them. Of these patients, 30 showed evidence of bilateral involvement and in the other 8 the limbs only on one side were involved. Operative intervention in 19 of the former resulted in 4 recoveries, and 6 of the patients with unilateral decerebrate attitudes survived after removal of the hematomas. In a recent report of epidural hemorrhages in children, Campbell and Cohen[4] mentioned the presence of decerebrate attitude in 4 patients who recovered following removal of the clots. Nelson[18] discussed involvement of the brain stem in the presence of subdural hematoma with particular reference to disturbances in eye movements. Six cases were reported, and in 4 instances recovery followed evacuation of the hematomas. In no cases was the decerebrate attitude recorded, but the evidence of disturbance in function of midbrain and pontine structures seems clear. Although good results are not to be expected in all instances, there is sufficient indication, as shown in the few previous reports and our cases, that surgery should not be withheld even though there is evidence of impairment of function of midbrain and pontine structures.

As has been noted previously, only few observations relative to spinal fluid pressure or appearance were made in this series. The observations of Smyth and Henderson[23] on simultaneous measurements of the ventricular and spinal fluid pressures showed that the pressure in the lumbar canal is not necessarily an index of intracranial pressure. The experiments of Dill and Isenhour[7] demonstrated that it is the supratentorial hypertension as opposed to generalized increase in pressure along the cerebrospinal axis that is a factor in the production of pathological alterations in the brain stem. Others have pointed out that withdrawal of spinal fluid may increase the difference in pressures between the supra- and infratentorial spaces and

further impair the circulation of the midbrain and pons. It is believed that little additional information of diagnostic importance is to be gained by spinal puncture in the presence of the decerebrate attitude and that further harm could ensue from this procedure.

Inequality of the pupils and disturbances in their reactivity to light was observed in most of our patients. In many, paresis of one or more extraocular muscles was also noted. However, it was not possible, from these studies, to determine whether alterations in function resulted from disturbance along the course of the 3rd and 6th cranial nerves or at their nuclei of origin. One patient had a residual of visual field defect which could not be attributed to involvement of the optic radiation by tumor or direct injury to the temporal lobe. It seems likely that this could be the result of infarction of the calcarine cortex, as demonstrated first by Adolf Meyer.[14] This phenomenon has since been discussed and demonstrated in pathological specimens by a number of observers.[1,8,16,20,21] Maltby[13] has reported the appearance of visual field disturbances in the course of subdural hematoma with subsequent recovery after evacuation of the subdural collections.

Three methods of treatment have been suggested for the relief of the effect of the temporal pressure cone on the midbrain. Foremost among these is the prompt evacuation of the offending mass by a suitable surgical procedure. This was carried out in 18 of our cases. In 8, liquid subdural collections were evacuated through simple trephine openings and in the case of the abscess, 60 cc. of pus were aspirated through a ventricular cannula. In the remaining 9 cases, osteoplastic craniotomies were made and the hematomas or tumors removed under direct vision. A second procedure was first suggested by Vincent, *et al.*[25] who mentioned the possibility of amputating the swollen temporal lobe, the medial aspect of which had herniated through the tentorial incisura. In effect, this was carried out in 1 patient of this series who suffered a contusion and dissolution of a temporal lobe as a result of trauma. In this instance, as a procedure of desperation, the pulpified temporal lobe was aspirated and irrigated out through two ventricular cannulas. In retrospect, it would probably have been a more sound surgical procedure if an open craniotomy had been done and the temporal lobectomy performed under direct vision. It seems to us that this procedure holds some possibility of effecting improvement in certain instances of severe cerebral trauma providing the affected side can be identified prior to the operation.

The third procedure that has been suggested is that of relieving the constricting ring formed by the free edge of the tentorium by sectioning that structure directly. Munro and Sisson[17] have recently reported the survival of some patients with severe cerebral trauma following this procedure. They believe that this not only provided relief of the direct compression of the midbrain by the edge of the tentorium, but also released cerebrospinal fluid dammed up under pressure in the subtentorial space. We have sectioned the tentorium in 3 instances of severe cerebral trauma wherein signs of decerebrate attitude were present without benefit.

It should be emphasized that any sign indicative of midbrain dysfunction should be a signal for immediate definitive surgery. One cannot foretell when the alterations in the midbrain structures will become irreversible and in delay the opportunity for obtaining benefit from operative intervention may be lost.

SUMMARY AND CONCLUSION

1. It seems well established that the decerebrate state associated with supratentorial space-taking lesions is a result of impairment of circulation in the brain stem secondary to herniation of the medial aspect of the temporal lobe through the incisura tentorii (the temporal pressure cone).

2. Nineteen cases are reported wherein recovery from the decerebrate state followed appropriate surgical procedures.

3. It is emphasized that any sign indicative of midbrain dysfunction occurring during the course of supratentorial space-taking lesions should be a signal for immediate definitive surgery.

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HYDROCEPHALUS FROM OVERPRODUCTION OF CEREBROSPINAL FLUID

(AND EXPERIENCES WITH OTHER PAPILLOMAS OF THE CHOROID PLEXUS)*

EDGAR A. KAHN, M.D., AND JOHN T. LUROS, M.D.
Department of Surgery, Section of Neurosurgery, University Hospital, Ann Arbor, Michigan

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PAPILLOMAS of the choroid plexus are rare tumors. There were but 12 (0.6 per cent) in Cushing's series of 2023 intracranial tumors. This has been the approximate percentage in other large clinics. We are presenting our series of 7 of these tumors because one case seems to prove beyond a doubt the commonly held view that hydrocephalus can on occasion be caused by an overproduction of cerebrospinal fluid.

In the excellent monograph on the pathology of hydrocephalus by Dorothy Russell[4] the three generally accepted ways in which hydrocephalus can be produced are clearly stated: "first, through over-secretion from the plexuses; secondly, through the interposition of an obstruction at some point in the cerebro-spinal pathway; or, thirdly from impairment of absorption."

It is Doctor Russell's[5] belief that though this first method of the production of hydrocephalus may exist, there is not as yet a well enough documented case to give absolute proof that hydrocephalus can result from the overproduction of cerebrospinal fluid alone.

CASE REPORTS

Case 1. R.W., a 20-year-old housewife, entered the hospital in July 1946 because of headaches of 5 years' duration. They had been particularly severe during and after a pregnancy which had terminated normally 3 weeks before.

Examination. There was papilledema of 4 D. with hemorrhages. Visual fields showed concentric contraction. Otherwise, the neurological findings were normal. X-rays of the skull were entirely normal.

Ventriculography revealed marked symmetrical dilatation of the ventricular system, with air in the 4th ventricle and in the cisterna magna (Fig. 1). There seemed to be a small amount of air in the cisterna interpeduncularis. There was a mass the size of a walnut in the region of the glomus of the choroid plexus in the left lateral ventricle (Fig. 2).

Clinical Diagnosis. The case was discussed with Dr. Max M. Peet, whose opinion was that this was a papilloma of the choroid plexus with an overproduction of cerebrospinal fluid. The operator (E.A.K.), however, wished to rule out a lesion of the posterior fossa which might be producing a ball-valve action. It was decided, there-

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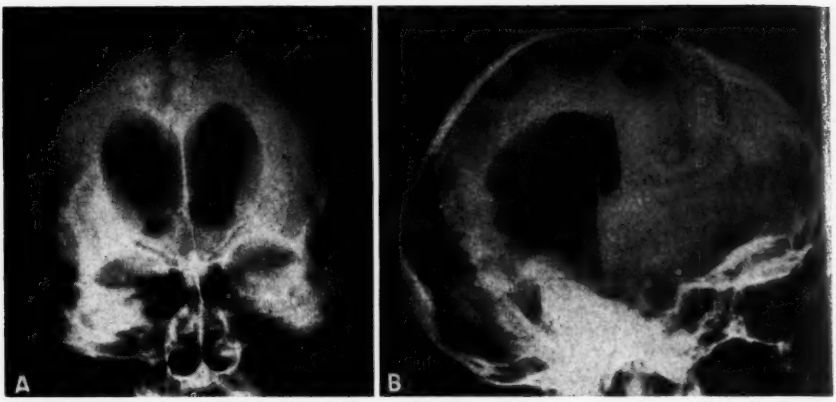

FIG. 1. *Case 1.* (A) Ventriculogram showing symmetrical dilatation of the ventricular system. (B) Browdown lateral ventriculogram demonstrating air in the 4th ventricle and cisterna magna.

fore, that the posterior fossa should be explored first and, should this be normal, the mass would then be removed from the left lateral ventricle.

Operation, Aug. 16, 1946. The cerebellar approach was made through a curved transverse incision. The occipital bone was of usual thickness. The cisterna magna was exceedingly large; its arachnoid appeared normal. The tonsils of the cerebellum were in normal anatomical position. The 4th ventricle was entered and CSF could be seen coming from the aqueduct of Sylvius. The cerebellar hemispheres appeared normal and were not needled. The wound was closed in the usual manner. It was now believed certain that the significant lesion lay in the left lateral ventricle. The patient was immediately placed on her side and an osteoplastic flap was turned down, centering over the left parietal eminence. A convolution was selected which was thought to be just posterior to the postcentral gyrus and above the supramarginal gyrus. An opening was made here into the lateral ventricle. A tumor about the size of a walnut, yellowish, quite smooth, and firm in consistency was seen arising from the choroid plexus itself. The entire tumor was removed, but some choroid plexus was left in the temporal horn.

FIG. 2. *Case 1.* Lateral view demonstrating neoplasm in region of the glomus with no evidence of obstruction. This is substantiated by air in the cisterna magna.

Microscopic Diagnosis. Papilloma of the choroid plexus (Fig. 3). The choroid plexus, containing psammoma bodies, from which the tumor had arisen was evident histologically (Fig. 3B).

Course. There was a marked receptive aphasia for several weeks but this soon disappeared. The papilledema

cleared and there were no residual neurological signs. The patient is entirely well 5 years postoperatively except for occasional headaches which she states are nothing "compared to the ones before operation." She has since had another child, who is now 3 years old. The patient is pregnant again at the present time.

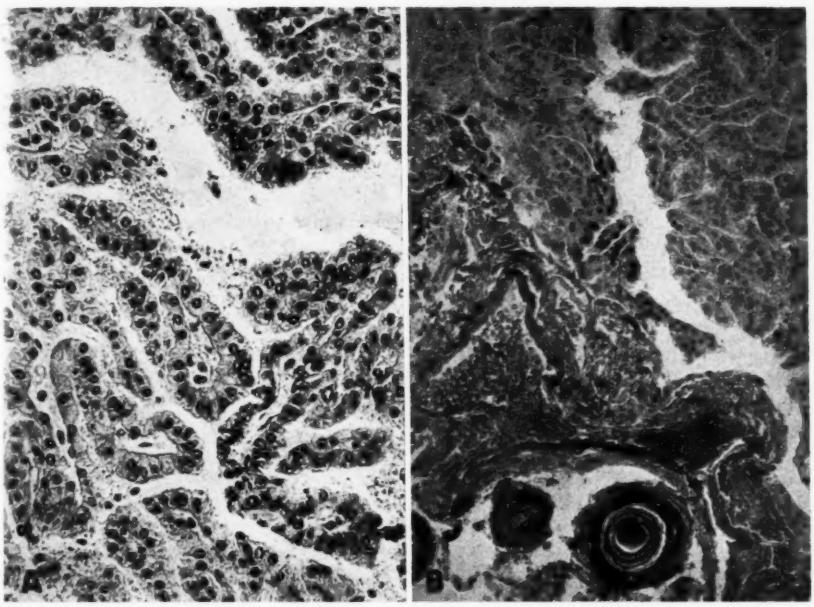

FIG. 3. *Case 1.* Photomicrographs of choroid plexus papilloma of the left lateral ventricle.

Discussion. In Case 1 a symmetrical dilatation of the entire ventricular system was evident. Air was present in the cisterna magna in large quantity and some appeared to be in the cisterna interpeduncularis as well. This shows that an obstructive hydrocephalus was not present, a fact also borne out by exploration of the 4th ventricle.

It is believed that nothing was done to open the communicating channels as no radical search was made beneath or around the cerebellar hemispheres, a procedure which could possibly have aided the cerebrospinal fluid in reaching the surface of the cerebral hemispheres. Again, nothing was done to improve the absorbing mechanism and the adding of blood to the cerebrospinal fluid might conceivably have diminished its absorption.

Since all symptoms of increased intracranial pressure have been absent for 5 years following excision of a papilloma of the choroid plexus of a lateral ventricle, and nothing further was accomplished by the operative procedures, it must be assumed that the hydrocephalus was caused in the first

place by an overproduction of cerebrospinal fluid. The tumor undoubtedly functioned as a tremendously hypertrophied choroid plexus.

Case 2. D.J., a 2-year-old girl, entered the hospital June 2, 1950 with a 2-week history of ataxia, dragging of the left leg, lethargy, headaches, nausea, vomiting, and generalized tremors of the extremities. A left convergent strabismus developed 2 days before admission.

Examination. She was a restless, irritable child who was unable to sit or stand by herself. The head was definitely hydrocephalic and emitted a cracked-pot sound on percussion. There was bilateral papilledema. A left 6th nerve palsy was present. There was marked ataxia and an intention tremor of the left upper extremity with athetoid movements. X-rays of the skull showed evidence of increased intracranial pressure. Ventriculograms showed a marked displacement of the ventricular system to the left with a widely dilated left lateral ventricle.

1st Operation. On June 6, 1950, a right temporal craniectomy, 3 cm. in diameter, revealed a large vascular subcortical tumor involving the temporal lobe. Because of the extent of the lesion and marked operative hemorrhage, only a biopsy was done. It was the operator's opinion that the tumor was a glioma.

Pathological Diagnosis. Papilloma of the choroid plexus.

2nd Operation. One month later, because of the benign microscopic appearance of the tumor, a second operation was performed with further removal of the growth. Again because of severe hemorrhage, the operation was abandoned after considerable tumor had been removed.

Course. The patient did well and was discharged home 2 weeks after operation.

She returned to the hospital 2 months later. There was improvement in her walking. A left hemiparesis was present. Babinski's sign was bilaterally positive. She was started on irradiation therapy in the right and left lateral mid-skull fields, receiving 100 r. to two fields per day for a total of 2000 r. per field. Her condition seemed to deteriorate throughout her stay in the hospital. The last x-ray treatment was given on Nov. 16, 1950.

She was brought back to the hospital on Dec. 10, 1950, apparently moribund. A ventriculostomy tube was placed in the left lateral ventricle for 5 days. Ventriculograms showed little change from previous examination. She was discharged on Jan. 5, 1951, just able to sit up.

Two months later the patient returned to the hospital remarkably improved to the extent that she could stand and walk with support. Though the decompression was bulging, it was thought that the tumor might have been sufficiently reduced in size by x-ray therapy to make removal feasible. Accordingly, ventriculography was again performed. In comparing the ventriculograms with those taken just after irradiation therapy, the actual tumor outline could still be seen and had not changed in any way.

The patient returned home and 8 days later began showing signs of increasing intracranial pressure. She re-entered the hospital moribund and died April 10, 1951.

Autopsy. A massive infiltrative papilloma of the right temporo-occipital parietal area projected into the lateral ventricle, but remained entirely subependymal, as far as could be determined (Fig. 4). The tumor seemed to be separated from the choroid plexus of the right lateral ventricle by ependyma so that it could not be determined for certain from where this typical papilloma arose. Both foramina of

Monro were patent and the 4th ventricle was dilated. There was no evidence of obstruction of the ventricular system.

Microscopically the papilloma showed no definite evidence of x-ray change in the sections examined; in fact, it appeared generally more cellular than the specimens taken at biopsy before x-ray treatment was instituted (Fig. 5).

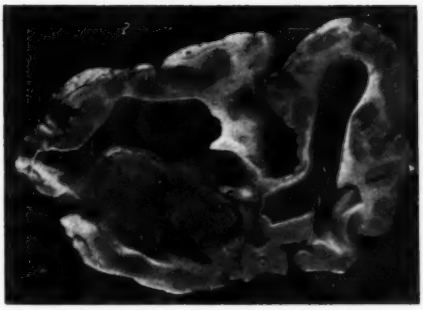

FIG. 4. *Case 2.* Coronal section showing that the tumor was apparently entirely subependymal. Choroid plexus is seen but whether the neoplasm arose from its undersurface could not be determined with certainty.

Discussion. Van Wagenen[6] reported a papilloma of the choroid plexus of the lateral ventricle in a girl of 3 months. The neoplasm was histologically similar to that in our case 2, though smaller and noninfiltrative in character. After a biopsy of the lesion was done, x-ray therapy was given. At a second operation the tumor appeared to be smaller

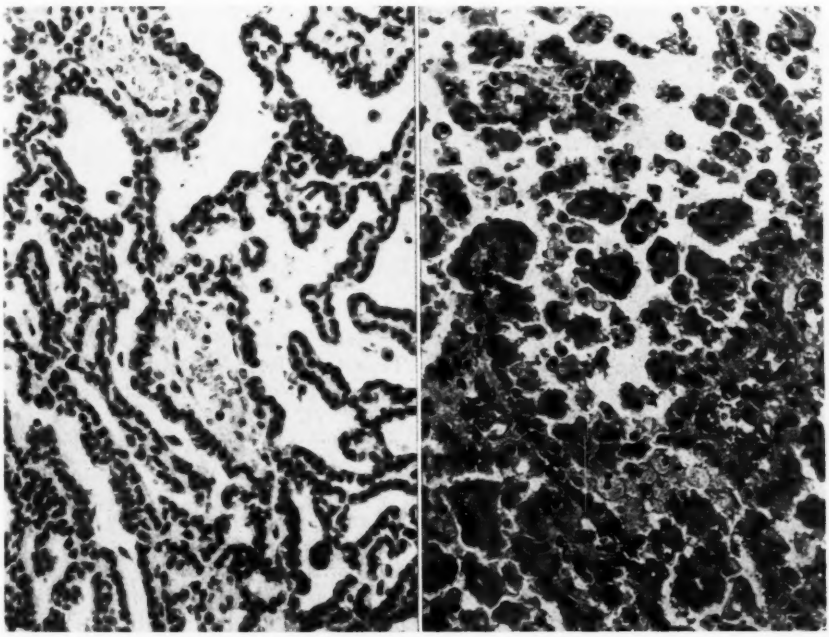

FIG. 5. *Case 2.* (A) Biopsy of tumor showing typical picture of a choroid plexus papilloma. (B) Tumor at autopsy. Whether this is postirradiation effect is questionable.

and less vascular and was believed to have been totally removed. The child died 2 years later, but the cause of death is unknown.

In our patient, following decompression and two partial excisions of the tumor, there was little change in condition. X-ray therapy was given and 8 days following the last treatment the child was continuing to go downhill. Then a little over 2 months after the last x-ray treatment, she started to improve. The reason for this is difficult to explain since the decompression had been present for 9 months and the lesion as shown by ventriculograms did not seem to have changed in size.

It might be postulated that at this late date an oversecretion of cerebrospinal fluid had been reduced by x-ray. This theory, however, is scarcely tenable since a communication between the tumor and the ventricular system was not obvious. The marked hydrocephalus found here in the absence of ventricular obstruction may have been due to obstruction in the communicating channels or the absorptive mechanism, though this was not demonstrable.

Case 3. A.S., a 5-month-old male infant, was admitted because of progressive enlargement of the head. The child was thought to be normal in all other respects.

Examination was completely negative except for moderate hydrocephalus. There was no bulging of the fontanelles. A ventricular tap was performed and the cortex was judged to be about 1 cm. in thickness. Methylene blue was instilled and recovered by the lumbar route. A ventriculogram disclosed evidence of a tumor of the 3rd ventricle.

Operation. On July 23, 1948 a right temporoparietal osteoplastic craniotomy was performed. Exploration through the right lateral ventricle revealed the tip of a solid tumor lying in the posterior part of the 3rd ventricle. Total removal was impossible, so that a biopsy was taken and the incision closed.

Pathological Diagnosis. Well differentiated papilloma of the choroid plexus.

Postoperative Course. The patient never fully rallied, having frequent bouts of hyperthermia. His course continued downhill and respirations ceased on the 21st postoperative day. Permission for autopsy was denied.

Case 4. R.W., a 19-month-old boy, had been well until September 1950, when he struck his head on a cement sidewalk. Three days later he began to vomit and this was said to be projectile in type. One week later the gait was noted to be slightly ataxic, and he then entered the University Hospital.

Examination. There were no signs of increased intracranial pressure. The optic disks were sharply outlined. On lumbar puncture the pressure was 150 mm. of water, but the total protein was 140 mg. per cent.

Course. He soon became symptom free. There were no other abnormal neurological findings, and he was discharged.

Six weeks later staggering occurred, and he was taken to another hospital for study. A generalized weakness and lack of coordination were noted. Lumbar puncture revealed normal pressure and a protein of 246 mg. per cent. Ventriculography on Nov. 24, 1950 revealed suggestive evidence of a tumor of the 4th ventricle. A medulloblastoma was suspected and x-ray therapy advised.

Readmission. The patient was returned to University Hospital on Dec. 2, 1950.

He was extremely ill and could no longer be aroused. A catheter was placed in the right lateral ventricle. Ventriculography showed definite evidence now of a tumor of the 4th ventricle.

Operation. Following 2 days of ventriculostomy drainage there was no improvement in the child's precarious condition, and a suboccipital craniectomy was performed. A large reddish-gray vascular tumor was removed from the 4th ventricle, except for a small amount that infiltrated the obex and extended into each lateral recess.

Pathological Diagnosis. Well differentiated papilloma of the choroid plexus.

Course. Convalescence was surprisingly good, and 1 year postoperatively the child seems normal in all ways. Because of the adult histological character of the growth, x-ray therapy was not given.

Discussion. Case 4 shows that a papilloma of the choroid plexus of the 4th ventricle in a child cannot be differentiated clinically from a medulloblastoma. A cerebellar astrocytoma that shows no localization by symptomatology or ventriculography can also mimic a medulloblastoma if its onset is comparatively acute. We are therefore opposed to x-ray therapy, before a lesion has been verified histologically, on the grounds that it is probably a medulloblastoma.

Case 5. V.A.K., a 40-year-old male, entered the hospital complaining of severe generalized headaches for the past 3 years. Three months before admission, he had had blurring of vision, diplopia, nausea, and vomiting.

Examination showed bilateral papilledema and a 6th nerve palsy on the right. There was no facial weakness. Diminution of auditory acuity was noted on the right. There were no signs of cerebellar disturbance. X-rays of the skull were normal. Ventriculography revealed evidence of an obstructive lesion in the posterior fossa.

Operation. A suboccipital craniectomy was performed, disclosing a reddish tumor in the 4th ventricle lying just cephalad to the obex. The tumor was removed in a piece-meal fashion until the aqueduct of Sylvius was exposed, and there was a free flow of cerebrospinal fluid through the aqueduct. The neoplasm was the size of a walnut and had infiltrated the medulla.

Pathological Diagnosis. Papilloma of the choroid plexus.

Postoperatively the patient never gained consciousness and expired 2 days later. Postmortem examination was not permitted.

Case 6. O.K., a 36-year-old male, was admitted on Nov. 23, 1933 with the history of deafness in the right ear for the past 5 years, and dysarthria and dysphagia for the past 6 months. Three months before admission there had been blurring of vision and ataxia.

Examination. There was bilateral papilledema. There was no sensory disturbance in the distribution of the right 5th nerve although the corneal sensation was a trifle less acute on the right as compared to the left. An almost complete peripheral right facial palsy was present. There was deviation of the soft palate to the left on phonation, and complete paralysis of the right vocal cord. X-rays of the skull showed irregular destruction of the right petrous ridge, and clouding of the mastoid cells on the right.

A biopsy of the lesion through the right middle ear was reported "an atypical papilliferous growth with the papillae and intervening spaces lined by a single layer

of cuboidal or columnar epithelium. The papillae are vascular and in some areas are indistinguishable from the choroid plexus."

Operation. A suboccipital craniectomy was performed, with disclosure of an extensive tumor lying in the right cerebellopontine angle. It was composed in large part of small cysts containing fluid varying in color from yellowish to dark green. This mass invaded the hemisphere of the cerebellum and appeared to pass through the incisura of the tentorium. Because of hemorrhage, it was possible to perform only a partial removal of the tumor.

Pathological Diagnosis. Papilloma of the choroid plexus.

Course. The patient made an uneventful recovery and was discharged on the 18th postoperative day. He never again was able to work and died 2 years later outside the hospital.

Discussion. An almost identical lesion in a man aged 26 was reported by Berlin.[1] The tumor had been considered to be a papilloma of the choroid plexus, but was finally diagnosed as a ceruminous adenoma involving the cerebellopontine angle. This case is unique and is mentioned only so that it can be considered in the differential diagnosis.

Case 7. J.K., a 47-year-old male, entered the hospital because of frontal headaches, of 2 months' duration, which radiated to the occiput. He had had two generalized convulsions and staggering during this period.

Examination. Significant findings were ataxia with falling to the right and bilateral papilledema. X-rays of the skull were normal. Ventriculograms indicated a right-sided posterior fossa lesion.

1st Operation. On April 8, 1936, a suboccipital craniectomy was performed. A grayish-black tumor, larger than a golf ball, was seen on the surface of the right cerebellar hemisphere. It was thought to be a meningioma though it had no dural attachment, and the entire tumor was excised grossly.

Pathological Diagnosis. Papillomatous adenocarcinoma of the choroid plexus.

Course. Convalescence was uneventful, and the patient was discharged 10 days postoperatively. He soon resumed his work in a factory.

One year later he returned to the hospital because of a recurrence of his symptoms of 2 weeks' duration. He was extremely ill and was immediately taken to the operating room.

2nd Operation. The old incision was reopened. A large cyst filled with dark brownish fluid, as well as an olive-sized blackish granular tumor on the inferior lateral surface of the tentorium on the right were removed.

Pathological Diagnosis. Recurrence of papillomatous adenocarcinoma of the choroid plexus.

Course. The patient withstood the operation remarkably well and his convalescence was surprisingly smooth. He was discharged on the 14th postoperative day.

He again resumed his work in a factory for at least 9 months. He died of recurrence 16 months postoperative. Autopsy was not performed.

Discussion. This was the only case in our series where a papilloma of the choroid plexus was frankly malignant.

SUMMARY

The conception that hydrocephalus can be produced by an overproduction of cerebrospinal fluid is proven by Case 1.

Six cases of benign papilloma and 1 of adenocarcinoma of the choroid plexus are presented. Two arose from the lateral ventricle, 1 from the 3rd ventricle, 2 from the 4th ventricle, 1 in the cerebellopontine angle, while the adenocarcinoma seemed to arise from the cerebellum itself. These neoplasms are reported[2] as occurring most commonly in the lateral ventricle during the first decade of life, and in the 4th ventricle during the 2nd, 3rd and 4th decades.

Surgical experience with this tumor started with Bielschowsky and Unger in 1902.[3] Since that time less than 100 choroid plexus papillomas have been reported, the majority having been disclosed at autopsy. Of the patients with papillomas that were removed surgically, about one half survived the immediate postoperative period.

In our series, only 1 patient has a survival period of 5 years and is assumed to be cured. One patient is alive 1 year postoperative and has no symptoms of recurrence. Another lived 9 months postoperatively and has recently died. Two patients survived for 2 years and have died, most likely from recurrences of their neoplasm. Two died in the immediate postoperative period.

Weinstein[7] stated that these tumors are usually demarcated if not encapsulated, and this has been our experience. In spite of their benign character, however, their location in recesses of the 4th ventricle and their adherence to the brain stem usually preclude total removal.

Deep roentgen therapy has been used so infrequently that its effectiveness cannot be determined adequately. One would hardly expect, however, such well differentiated neoplasms to respond to irradiation therapy. It is possible that any beneficial effect of x-ray may be attributed to diminishing the overproduction of cerebrospinal fluid.

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THE EFFECTS OF INTRACAROTID DIODRAST*

ELDON L. FOLTZ, M.D.,† L. B. THOMAS, M.D., AND
A. A. WARD, JR., M.D.
Division of Neurosurgery, University of Washington School of Medicine, Seattle, Washington

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THE increasing popularity of Diodrast angiography since 1938 has been motivated by the obvious clinical value of this procedure, but it is surprising that no investigations of the action of Diodrast on cerebral function have been undertaken until recently. The occurrence of complications following cerebral angiography has been poorly documented in the past and, indeed, has often gone unrecognized. However, the recent widespread enthusiasm for angiography has resulted in an increasing awareness of the clinical sequelae of this procedure. Physiological investigation into the causes of these sequelae has been almost totally lacking. For these reasons, it seemed pertinent to study the effects of intracarotid Diodrast.

METHODS

Experiments were carried out in 12 monkeys (*Macacus rhesus*), 4 cats, and 10 humans. Of the 12 monkeys, 6 were anesthetized with Dial,‡ 1 with pentobarbital, and in the remaining 5 the surgical exposure was carried out under pentothal anesthesia with the experimental recording being done under local anesthesia in the neck. One of these monkeys was paralyzed with dihydro-beta-erythroidine hydrobromide.§ All of the cats were anesthetized with Dial.‡ In the humans the recording was carried out under local anesthesia in 5 cases, with intravenous pentothal in 4, and with vinethene-ether in 1 case.

With the exception of 5 human cases where the Diodrast was introduced by percutaneous puncture of the carotid artery, all carotid injections in the remaining humans and in all the experimental animals were accomplished by means of an inlying polyethylene catheter. In the animals a PE 20 polyethylene catheter was introduced into the surgically exposed common carotid artery and usually threaded up the internal carotid artery to the base of the skull. In humans a PE 50 catheter was used in the same manner.

The electroencephalograms were recorded on 8-channel Grass or Offner instruments using small needle electrodes inserted into the scalp. Bipolar recording was used throughout, and the electrode placements were the same in all cases. The arm-to-arm electrocardiogram was likewise recorded on the EEG. Continuous recording of the cerebrospinal fluid pressure was carried out in animals by means of a

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† Post-doctorate Research Fellow, United States Public Health Service.

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nylon catheter ligated in the lower end of the dural sac after the tip of the catheter had been threaded up to the mid-thoracic level. This catheter was directly connected to a Statham strain gage whose output was recorded by a carrier-wave amplifier and ink writer.

Changes in the caliber of pial vessels were observed in certain animals after wide bilateral exposure of the cerebral hemispheres, by a modified Forbes window inserted into a small trephine hole, and by a lucite calvarium. In the latter instance the entire bony calvarium of a monkey was aseptically removed. An acrylic plate, molded to the removed calvarium, was inserted in position by multiple wires. In addition to visual inspection, high speed color motion pictures were taken of the pial circulation during Diodrast injection.

Thirty-five per cent and 70 per cent Diodrast solutions were both used in each case except in two humans where only 35 per cent solutions were used. The order and timing of the injections of the different strength solutions were so arranged that the effects observed were clearly a direct result of the immediately preceding injection. The temperature of the injected Diodrast was maintained by a controlled temperature water bath. Cool solutions were maintained at 70°F., and warm solutions at 99.8°F. The injection time was kept constant for each case. The volume of Diodrast per injection was 2½ cc. for cats, 4 cc. for monkeys, and 10 cc. for humans. Adequate precautions were taken to maintain sterility and to guard the Diodrast solutions against light. Stellate blocks, when performed, were carried out with 1 per cent monocaine, using minimum volumes to obtain maximal homolateral pupillary constriction.

RESULTS

The effects of intracarotid Diodrast on the brain seem to be twofold. First, a direct vascular effect and, secondly, a neuronal or cellular effect. The vascular effect is a short, severe vascular spasm followed by a longer lasting vascular dilatation. The neuronal effect may be a result of direct toxic action of the drug on the brain, or possibly a combination of this and the vascular changes.

Vascular Effects. The cerebral vascular effects were studied by direct visualization of the cortex during the Diodrast injections and also by continuous measurements of the intracranial pressure during and following Diodrast injections. Direct cortex visualization showed, in all cases, a severe vasospasm of the pial arterioles starting at the midpoint of the injection. This began as a high speed, repetitive series of momentary arteriolar constrictions which gave a fluttering appearance lasting only a few seconds. This was replaced by cortical blanching in which the dark veins stood out in startling contrast. This second phase always began during the end of injection and lasted for 60 to 90 sec., definitely after the completion of injection. This was followed by the third phase consisting of a cortical blush lasting 1 to 2 min. Both 35 per cent and 70 per cent Diodrast caused these changes, though changes induced by the 70 per cent solutions were always more severe. Injection of similar volumes of saline under identical conditions showed none of these effects.

The results of continuous recording of intracranial pressure changes dur-

ing Diodrast injections showed a constant pattern when room temperature Diodrast was used (Fig. 1A). The rapid initial pressure drop of 10 to 15 mm. of water during the terminal 2 to 3 sec. of injection corresponds to the observed vasoconstriction phase. Presumably this drop is secondary to the rapid and severe initial vasospasm. The rise in pressure immediately following this drop is transient and corresponds temporally to the vasodilation and

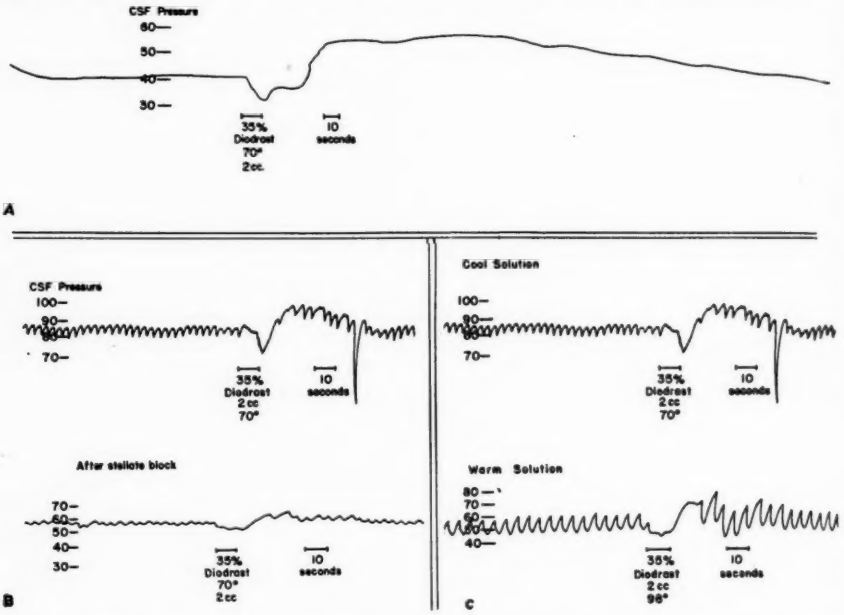

FIG. 1. Intracranial pressure responses to intracarotid Diodrast. (A) Usual response. (B) Effect of unilateral stellate block. (C) Effects of warm and cool intracarotid Diodrast.

cortical blush phases of the observed vascular effect. There was no prolonged effect on the CSF pressure beyond 5 to 6 min. after injection. In this aspect, 35 per cent solutions caused just as marked pressure changes as did the 70 per cent solutions.

To substantiate this correlation between the initial pressure drop and the initial vasospasm CSF pressures were recorded during intracarotid Diodrast injection before and after unilateral stellate block, since stellate block should alter changes that are of vasomotor origin. In all cases the initial pressure drop which was present before the stellate block was completely abolished after the stellate block (Fig. 1B).

Furthermore, since warm and cool solutions should theoretically have different effects on vascular spasm, pressure records during the injection of warm and cool Diodrast were compared. In the same animal there always

was a very definite difference in the pressure response. The cool (70°F.) Diodrast routinely produced twice as much initial fall in pressure as did the warm (99.8°F.) Diodrast (Fig. 1C). Frequently the secondary rise in CSF pressure was significantly greater following the injection of the warm solution than following the cool solutions. The opposite effect was never observed. These changes were never seen after injection of warm or cool saline.

EEG Effects. The neuronal effects were studied by electroencephalograms taken during and following the injection of Diodrast. The acute EEG changes have been varied and exceedingly complex to analyze, apparently due to the large number of variables involved. These include the presence or absence of CNS lesions, the depth and type of anesthesia, the strength of the Diodrast solution and the temperature of the injected Diodrast as well as concomitant cardiac and respiratory effects. A statistical analysis of the EEG changes is thus not possible. The effects of 35 per cent and 70 per cent Diodrast solutions differed only in the degree of severity of the reaction. Thus both solution strengths produced similar EEG changes, differing only quantitatively. The observed acute effect on the EEG can be divided into two broad groups, those in which a negative effect occurred, and those in which a positive effect was produced. Negative effect as used here means the reduction in amplitude of rhythmic discharges, or in the case of recurring transients such as spikes, a reduction in either amplitude or frequency. A positive effect denotes the production of new wave forms, increase in amplitude of rhythmic discharges, or in the case of recurrent transients such as spikes, an increase in either amplitude or frequency.

Negative effects on cortical electrical activity were exhibited in two ways: (1) by flattening of all wave forms; and (2) by loss of spikes. Within this category generalized flattening of the EEG was most frequently seen (Fig. 2A). When present, it always started during the terminal half of the Diodrast injection and usually lasted 10 to 20 sec., though a duration of 1 or 2 min. occasionally occurred. The recovery periods were of variable duration and character, though almost all the EEGs returned to the pre-injection pattern within 20 min. When the EEG flattening occurred acutely during unilateral injection, the depression of cortical activity was bilateral, although the flattening was occasionally asymmetric. The EEG flattening involved all wave forms present at the start of injection, and occasionally was so marked that the cortical activity appeared almost isoelectric. In two instances chronic flattening of the EEG occurred and was always on the side of injection (Fig. 2B). In these cases hemiparesis occurred associated with marked flattening of cortical activity on the side of injection. In one animal the paresis cleared and the EEG returned to normal in 3 days. In the other, an epileptic monkey, the paresis cleared in 1 week, although the EEG still showed marked flattening on the side of injection 5 weeks later. Initial loss of cortical spikes occurred following Diodrast injection at least once in all epileptic monkeys (Fig. 3). If the spikes were bilateral the Diodrast injection

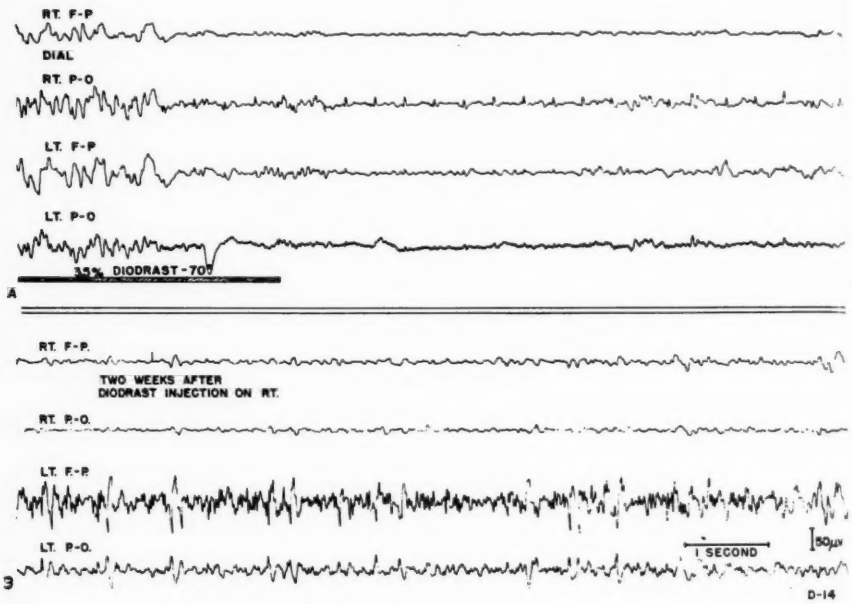

FIG. 2. EEG depression. (A) Acute flattening in all leads. (B) Chronic flattening on the side of injection.

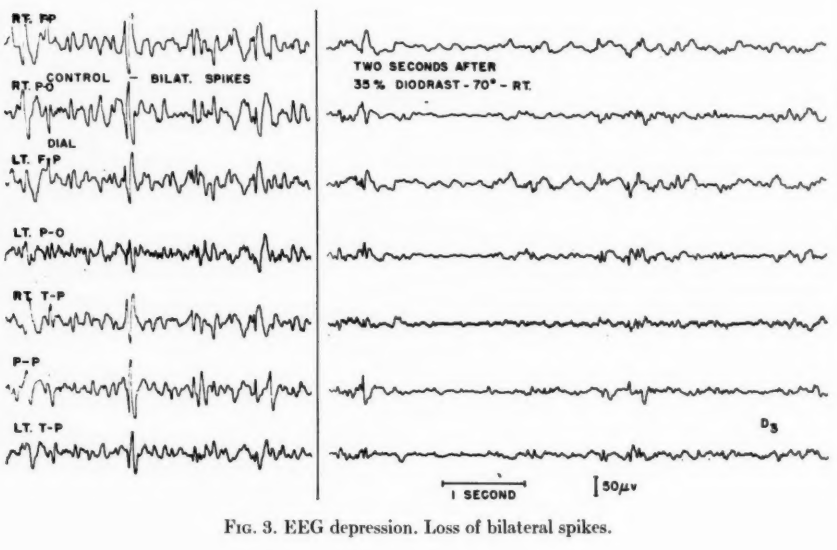

FIG. 3. EEG depression. Loss of bilateral spikes.

abolished the spikes on both sides as illustrated. In a lateralized spike focus loss of spikes occurred homolaterally. The loss persisted for 2 to 3 min. after the injection. It is of passing interest that a spike focus was abolished for 3 min. in one epileptic monkey during carotid occlusion for the purpose of closing the puncture wound after a series of Diodrast injections. Occlusion of the carotid artery prior to injection did not have this effect. The positive effects on cortical activity are divided into (1) augmentation of slow wave activity; (2) delayed bursts of spikey 14/sec. waves; (3) generalized increase

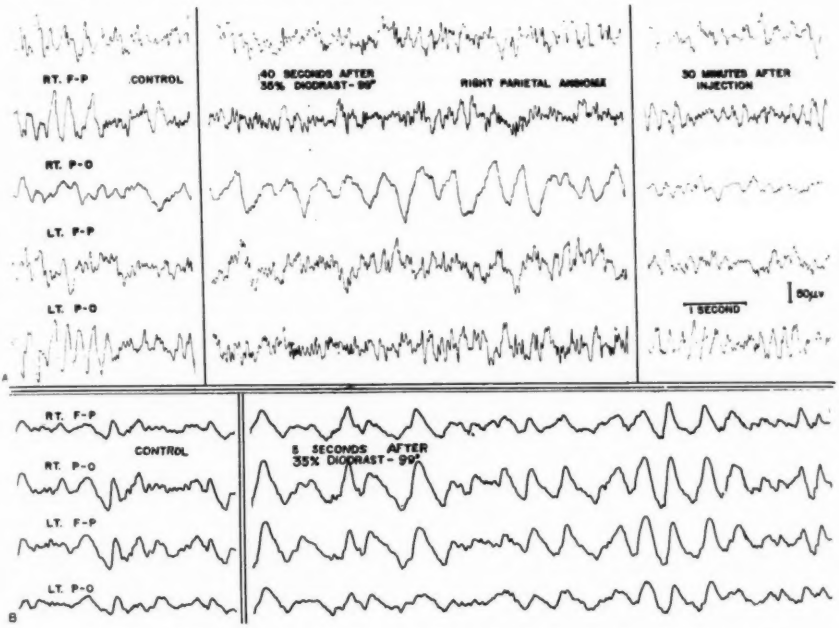

FIG. 4. EEG depression. (A) Augmentation of focal delta activity. (B) Augmentation of generalized delta activity.

in fast activity and spike production; (4) augmentation of spikes; (5) spike and dome activity; and (6) seizure discharges.

Augmentation of delta activity was a constant finding in cases showing slow waves in their control EEGs. This increase in slow wave activity persisted as long as 2 hrs. following injection. When these slow waves were focal, only focal augmentation occurred (Fig. 4A). When generalized delta activity was present, the augmentation was generalized (Fig. 4B). In Fig. 4A a slow wave focus is demonstrated in the right parietal region surrounding an intracerebral angioma. Following angiography a marked increase in the focal delta occurred lasting 30 min. The generalized delta activity present in the EEG of a sick monkey is shown in Fig. 4B, where a marked increase in the generalized slow wave activity occurred after Diodrast injection. It

should be pointed out that this augmentation of slow activity, which by the definition adopted falls into the class of positive effects, was apparently associated with a functional reduction in activity as judged clinically by impairment or loss of consciousness.

The homolateral production of delayed spikey waves at 14/sec. occurred frequently and is illustrated in Fig. 5A. These bursts were always on the side

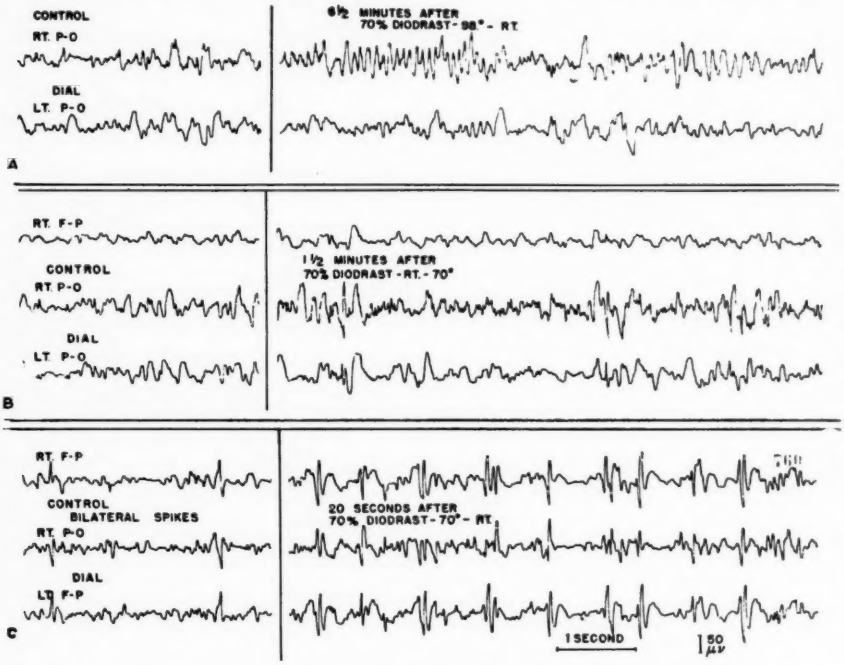

FIG. 5. EEG activation. (A) Delayed bursts of 14/sec. spikey waves. (B) Focal increase in fast activity, spike production. (C) Augmentation of spike activity.

injected and never appeared before 1 to 2 min. after injection, persisting intermittently for 1 to several min. These wave complexes were never seen in the control EEGs.

Homolateral augmentation of complex fast activity appeared often and usually started within 30 sec. following Diodrast injection, and lasted from 1 min. up to 1½ hrs. In some instances the augmented fast activity was quickly replaced by spikes. In others, unilateral spikes alone were produced immediately following injection with no antecedent fast activity. In epileptic monkeys exhibiting spikes in their pre-injection EEGs, these spikes may be augmented. It was possible to trigger these spikes by auditory stimuli on occasion. The human cases with pre-existing temporal lobe spikes or sharp waves consistently showed some augmentation of these abnormalities. Some

of these changes in the monkey are illustrated in Fig. 5B where homolateral spikes were produced as well as augmentation of complex fast activity in channel 2. In Fig. 5C marked augmentation of pre-existing spikes was produced in an epileptic monkey by injection of Diodrast. These augmented spikes approach a seizure discharge although no seizure occurred.

Spike and dome activity (Fig. 6A) was seen only in monkeys after intracarotid Diodrast. In these cases the injection produced 6 to 10 sec. of generalized flattening followed by a build-up period of complex wave patterns lasting 30 to 60 sec., culminating in a spike and dome discharge as illus-

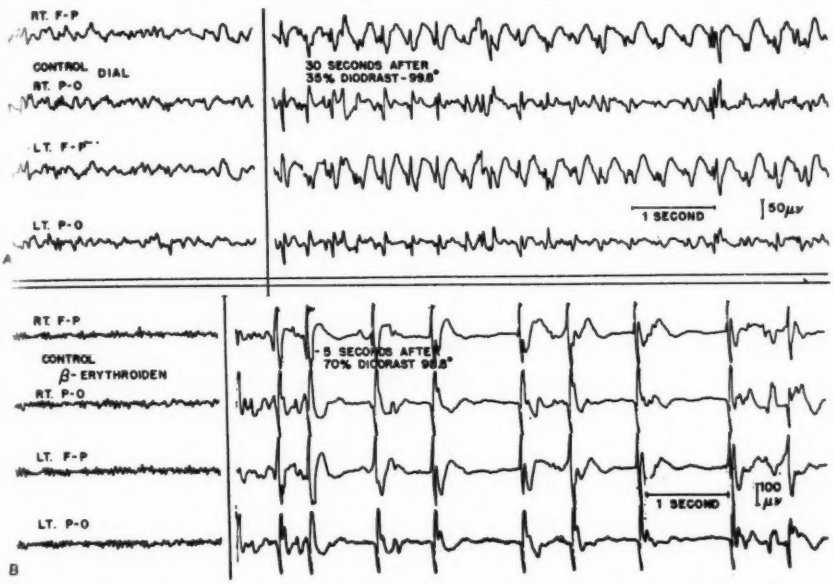

FIG. 6. EEG activation. (A) Production of spike and dome activity. (B) Production of seizure discharge

trated. In the experiment illustrated the animal was an epileptic monkey in which the cortical spikes had been abolished by a single injection of Diodrast 4 min. prior to this injection.

Seizure discharges were severe when they occurred. It is significant that in two instances clinical seizures took place in the presence of barbiturate anesthesia. The clinical seizures and the seizure discharges in the EEG always occurred almost immediately following the injection, and in only one instance was the seizure lateralized. The electrical recording of such seizures can be demonstrated in its entirety only in animals paralyzed with dihydro-beta-erythroidine hydrobromide, as shown in Fig. 6B.

It is impossible to determine what portion of these changes in neuronal activity is due to the already demonstrated vascular changes and what may be the result of the drug acting directly on the nerve cell. It has been demon-

strated that intracarotid Diodrast results in initial vasospasm followed by longer lasting vasodilatation, as judged both by direct visualization of intracranial vessels and by quantitative measurement of intracranial pressure. Furthermore, injection of cool Diodrast causes more vasospasm than warm, and both of these effects are minimized by unilateral stellate ganglion block. On the basis of these observations one might postulate that two effects exist: (1) a direct toxic action on the nerve cell; and (2) a protective vasospasm

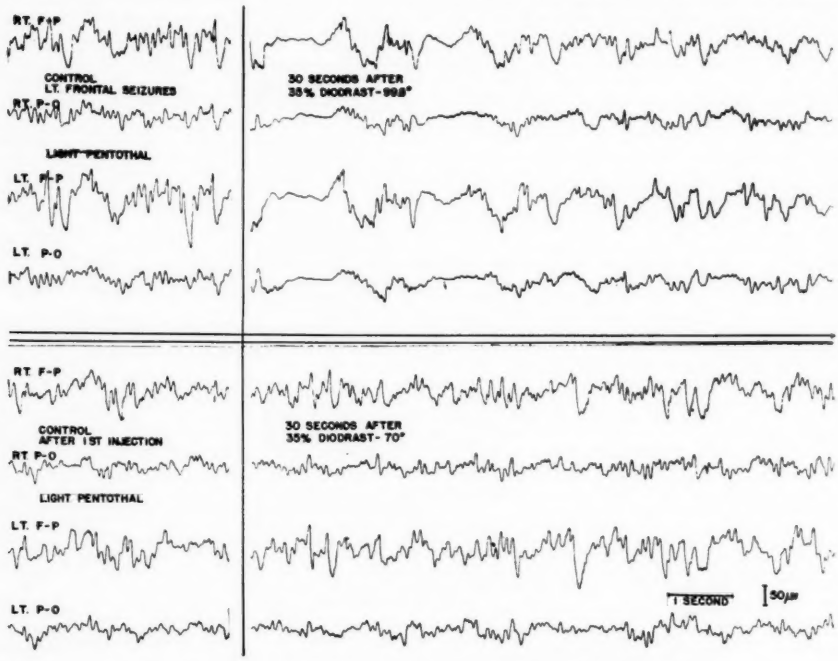

FIG. 7. Difference in neuronal effect of warm and cool Diodrast solution.

which minimizes the amount of toxic substance reaching the nerve cell in any given period of time. If this were the case, injection of warm solutions, which cause less vasospasm, should produce greater neuronal changes than injection of cool solutions. Likewise, blocking the protective vasospasm should also produce even greater toxic neuronal effects as judged by the EEG.

In Fig. 7 the effects of injection of warm and cool solutions of Diodrast are compared in a human epileptic patient under light pentothal anesthesia. The initial injection of warm 35 per cent Diodrast abolished the pentothal bursts, leaving the abnormal sharp and slow wave activity standing out in contrast. After the EEG had returned to its previous level 5 min. later, an injection of cool 35 per cent Diodrast produced only minimal changes. Thus,

injection of a warm solution, which produced only minimal protective vasospasm, allowed a greater amount of the drug to reach the nerve cell and produce toxic effects as judged by the EEG changes. The greater vasospasm produced by subsequent injection of the cool solutions protected the nerve cells and minimized these changes. This occurred in spite of a greater toxic action which might be anticipated due to the accumulated dosage. This has been a routine observation in all human and animal experiments when an EEG change was produced. Furthermore, all three of the seizure discharges produced in this series were produced only by warm solutions of Diodrast. Likewise, 90 per cent of all instances of augmentation of delta wave activity were the result of injection of warm solutions of Diodrast. These effects were

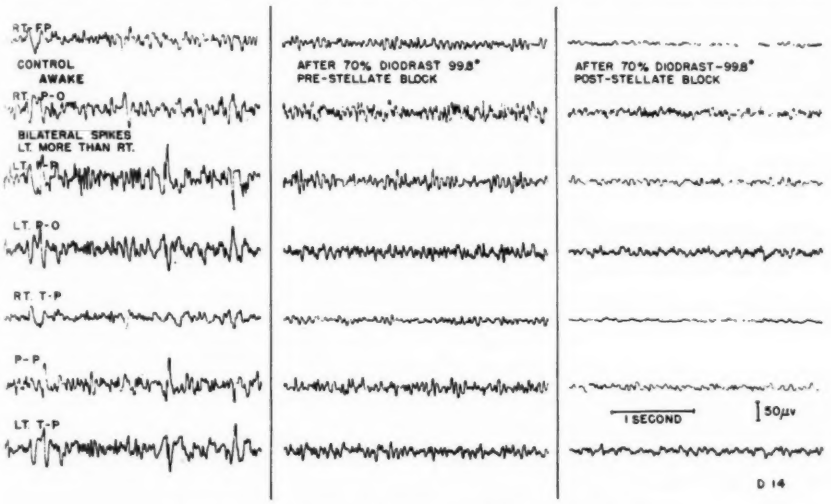

FIG. 8. Increased neuronal depression following stellate block.

never seen after injection of warm and cool solutions of isotonic saline which was carried out in every case.

In Fig. 8 initial injection of warm Diodrast in an awake, epileptic monkey produced minimal flattening of the EEG with abolition of spikes. Thus, injection of the warm solution reduced the protective vasospasm and caused a moderate direct toxic action on the neurones. After the EEG had returned to its previous level 10 min. later, a homolateral stellate block was performed. Reinjection of a warm solution of Diodrast now caused very striking EEG depression lasting 6 min. as illustrated, the spikes being abolished for 2 hrs. The only animals that died acutely following intracarotid Diodrast were two cats on which unilateral stellate blocks had been done prior to the injection. Thus stellate block minimizes the protective vasospasm and allows a greater concentration of dye to reach the tissues where its direct cytotoxic action can be demonstrated. However, it was found in other experiments that even

after homolateral stellate block, injections of warm solutions of Diodrast still caused somewhat greater EEG effects than cool solutions.

EKG Changes. Various EKG abnormalities were observed during and following the intracarotid injection of Diodrast. Fig. 9 summarizes some of these. In Fig. 9A there is vagal slowing for a single beat with loss of the "p" wave which occurred during the period of injection. Persistent bradycardia with intermittent loss of "p" waves may also occur as illustrated in Fig. 9B, this effect occasionally lasting as long as 2 min. These two effects were fairly common observations in both the human and monkey. In one monkey rhythmic ventricular extrasystoles occurred (Fig. 9C) over a period of almost 3 min. There is circumstantial evidence that these are the result of central nervous system changes mediated by the vagosympathetic system. The fact that these EKG changes occur more frequently with intracarotid than with

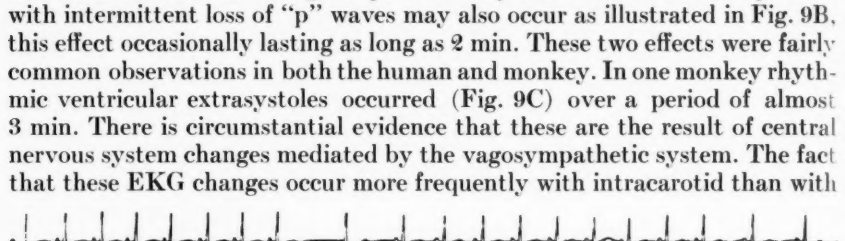

FIG. 9. EKG. (A) Vagal slowing and loss of "p" wave for one beat. (B) Persistent bradycardia with intermittent loss of "p" wave. (C) Production of rhythmic ventricular extrasystoles.

intravenous Diodrast would suggest that a direct myocardial action is not the cause. In all instances where no EKG effect was obtained in the present series, the injection was below the carotid bifurcation. This would suggest that these abnormalities are not mediated through the carotid sinus mechanism. It also suggests that these abnormalities are not due to a direct myocardial action, since the dilution factor is the same regardless of the level of injection into the carotid system. All injections through a catheter threaded up to the base of the skull resulted in some type of EKG or pulse rate abnormality, presumably due to the higher concentration of Diodrast reaching the brain.

Miscellaneous Effects. The occurrence of seizures, monoparesis and transient hemiparesis has already been described. Apparent reversal of a post-injection hemiplegia was produced by stellate block in one monkey. Homolateral dilatation of the pupil with conjunctival injection and tearing were routinely observed in all animal and human cases. This is doubtless due to Diodrast reaching these structures via the ophthalmic artery. In those instances where the injection was done by needle puncture below the bifur-

cation of the carotid artery in monkeys, swelling and edema of the neck muscles and soft tissues always occurred very shortly after the injection of Diodrast. This effect is due to Diodrast in the distribution of the external carotid artery and was never seen following injections of the internal carotid alone. Following percutaneous injection in the human, this swelling can be mistaken for local extravasation of blood or Diodrast. This might even explain the laryngeal stridor occasionally seen in humans which results from laryngeal edema. These distressing effects in the neck can be prevented by selective injection of the internal carotid artery only.

It has been observed that severe, unilateral head pain may occur in the awake human at the time of injection. In this series the pain was reported as being worse when cool solutions of Diodrast were injected. Likewise, the awake monkeys always reacted more severely to injections of cool solutions. Since it has been shown that such solutions cause maximal vasospasm, this further substantiates the belief that this pain is secondary to the vasospasm.

Hyperpnea is seen fairly frequently in both awake and anesthetized monkeys as well as humans. Respiratory arrest was infrequently seen in animals. Increased lethargy occasionally occurs following injection in both animals and humans. In this series this lethargy was most pronounced in humans with pre-existing CNS damage. No human death has occurred in the experience of the authors, but in this series there were 3 monkeys and 2 cats which died following intracarotid Diodrast. In both cats death occurred abruptly following immediate respiratory arrest at the end of injection. The monkeys expired at periods ranging from 12 to 48 hrs. after an experiment consisting of multiple Diodrast injections.

When any vasomotor or EEG effect was produced it was always more marked with 70 per cent than with 35 per cent Diodrast. On occasion, only the 70 per cent solution produced the changes described. It would appear that the effects are roughly proportional to the concentration of the dye. The evidence for cumulative effects on repeated injections is less clear. Marked individual variation in the tolerance to Diodrast was present, and in one monkey 400 mg./kg. of body weight was injected without permanent residua. This is four times the "equivalent human dose" as calculated by Heathcote and Gardner.[6] Factors influencing cumulative effects include type of anesthesia, presence of organic changes in the CNS, concentration and volume of Diodrast per injection, interval between injections, presence or absence of cardiorespiratory effects, and individual variation. In view of the multiplicity of factors, it is not surprising that no definite correlation could be established in this series between the total amount of Diodrast injected and the effects observed. In studying the various effects here described, any possible cumulative effects were felt to be eliminated. In spite of an attempt at detailed statistical analysis, no precise correlation can be drawn between CNS changes and total dosage. However, a crude qualitative impression exists that the described changes are somewhat greater following repeated injections.

DISCUSSION

In a recent monograph on carotid angiography based on over 2000 cerebral angiograms using Diodrast, Torkildsen[10] has listed some of the various complications that may occur, but has failed to determine their frequency by detailed analysis. That Diodrast angiography is not completely innocuous is indicated by the recent report of Dunsmore, Scoville and Whitcomb who report a 14 per cent incidence of complications in their series of 108 cases. They also point out that the previous literature emphasizes the relative safety of the procedure. Previous investigations regarding the mechanism of these complications in the use of Diodrast have been scanty.

The present investigation on monkeys and humans indicates that intracarotid Diodrast has two effects on the brain: (1) a direct toxic action on the nerve cell; and (2) a protective vasospasm minimizing the amount of toxic substance reaching the nerve cell in any given period of time. Angiospasm at the time of Diodrast injection has been previously described by Broman and Olsson[3] who observed that there was no pial circulation for 3 to 8 sec. after injection of the contrast medium. The present findings would agree with this except in detail. Vasoconstriction has also been observed by Holm[8] in the cranial circulation and by Edwards and Biguria[5] during femoral arteriography with Diodrast.

Broman and Olsson demonstrated marked changes in the blood-brain barrier after intracarotid Diodrast in animals, using the trypan blue technique. This and certain other dyes will not, under normal circumstances, pass through cerebral vascular membranes. Following endothelial damage the permeability is increased and the dye then stains the damaged portion of the brain. They illustrate that intracarotid Diodrast causes the injected hemisphere to stain a bright blue. These authors felt that the Diodrast damage to the brain in their series was a pure injury to the blood-brain barrier without edema, hemorrhage, necrosis or thrombosis. However, their evidence would indicate that some direct cytotoxic effect does exist since they describe increasing clinical signs in the presence of regressing changes in vascular permeability.

Using Evans blue, Bassett, Rogers and Cherry[1] demonstrated in dogs and rabbits that similar increases in the permeability of the blood-brain barrier were produced by Diodrast. They point out that pH of the injection medium is not a major factor and that the osmotic pressure of the injected solution is not solely responsible since injection of 20 per cent saline, which has the same tonicity as 35 per cent Diodrast, causes slightly less change in the permeability than does Diodrast. These authors, however, deny the existence of massive vasospasm.

Bloor, Wrenn and Margolis,[2] using copper phthalocyanine dye in rabbits, likewise demonstrated changes in permeability of cerebral vessels and showed pathological changes in endothelium and also in nerve cells. This latter finding is in direct contrast to the report of Kristiansen and Cammermeyer[9] who failed to observe any pathological changes in the brain following carotid

angiography with Diodrast. Bloor *et al.* also point out that EEG changes parallel the dye transfer and pathological changes. EEG changes somewhat similar to those reported here have also been described in dogs and humans by Heimburger and Freeman.[7]

The correlation between the alterations in vascular permeability and the EEG changes is not entirely clear. In the present experiments when the vasospastic element was minimized by stellate block and warm solutions, the immediate EEG changes were much more marked and occurred more rapidly than might be anticipated if these alterations in neuronal activity were due solely to increased vascular permeability. On the other hand, late effects, as judged by the EEG and clinical complications, might well be explained by both the direct cytotoxic effect and the changes in the blood-brain barrier, the relative contribution of each being unknown. That changes in the blood-brain barrier may occur without the development of cerebral edema has been pointed out by Broman and Olsson,[3] and this agrees with our observations that there is no late development of increased spinal fluid pressure.

Certain clinical applications seem warranted on the basis of our results. Warm solutions of Diodrast produced less vasospasm but greater EEG changes than cool solutions, suggesting that a greater cytotoxic effect was produced. Temperature alone is not the critical variable since neither warm nor cool intracarotid saline produces any vascular effect or EEG changes. At the present time we are not able to judge whether the increased activity of warm Diodrast is due to chemical activation or to some other factor. In any case, the warming of Diodrast to body temperature prior to injection would seem to be contraindicated.

Since the cerebral effects of intracarotid Diodrast are startlingly increased after stellate block, measures designed to minimize cerebral vasospasm during Diodrast injection are also contraindicated. Although better radiological contrast might be achieved by these measures, it would be at the expense of increased cellular damage. However, this does not alter the indications for stellate block after angiography in selected cases.

It should be emphasized that the changes here described do not fall into the category of changes seen clinically that are classified as "complications." It has already been reported that such complications representing major CNS damage do occur in about 14 per cent of clinical cases (Dunsmore, *et al.*[4]). However, clinical methods in current use are so crude that fine abnormalities of structure or function cannot be determined. It is these finer abnormalities caused by intracarotid Diodrast that have been described in this experimental series. Thus, the fact that major complications occur relatively infrequently should not obscure the fact that some diffuse damage including neuronal death may occur almost routinely as the result of Diodrast angiography. These possible hazards must therefore always be weighed against the information gained by angiography in any particular patient. The obvious solution would be a contrast medium that does not possess

the toxic properties of Diodrast. Various new substances are in preparation which will be screened by laboratory methods for possible use in carotid angiography.

CONCLUSIONS

1. Diodrast is far from an ideal contrast medium for cerebral angiography. Two primary effects of intracarotid Diodrast are demonstrated (a) a direct toxic action on the nerve cells; and (b) a protective vasospasm minimizing the cytotoxic effect.

2. Initial rapid vasoconstriction followed by longer lasting vasodilatation was demonstrated visually and photographically in monkeys. Quantitative continuous recording of spinal fluid pressure during angiography demonstrated an initial rapid fall in pressure followed by a longer lasting rise corresponding to the observed vasomotor changes.

3. Continuous recording of the electroencephalogram during intracarotid Diodrast in both monkeys and humans demonstrated multiple abnormalities which seem to be due to a direct toxic action of diodrast on the neurones.

4. Warm solutions of Diodrast produced less vasospasm than cool. Unilateral stellate block also abolished the phase of vasoconstriction. After this protective vasospasm had been minimized by either of these means, intracarotid Diodrast then produced far greater abnormalities in the electroencephalogram.

5. Some type of electrocardiographic or pulse rate abnormality was routinely produced in both monkeys and humans during angiography. These seem to be the result of central nervous system changes.

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TISSUE REACTIONS TO POWDERED TANTALUM IN THE CENTRAL NERVOUS SYSTEM*

ORVILLE T. BAILEY M.D., FRANC D. INGRAHAM, M.D., PRESTON S. WEADON, M.D. AND ANTHONY F. SUSEN, M.D.

Departments of Pathology and Surgery, Harvard Medical School, and the Neurosurgical Service of The Children's Medical Center, Boston, Massachusetts

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A SERIES of studies has been undertaken to determine the effects of radioactive tantalum (Ta^{182}) in the central nervous system of experimental animals under normal and pathological conditions. As a preliminary phase of this study, an attempt has been made to define the tissue reactions to powdered non-radioactive tantalum in various sites in the brain and spinal cord and to evaluate the differences in tissue behavior resulting from variations in the size of the tantalum particles.

Tantalum was introduced into surgery by Burke[2] in 1940 and has since been put to a variety of uses in that field. It has been successfully employed as plates, clips, foil, wire, gauze and powder. Although experimental studies have usually indicated that little reaction is elicited by tantalum in tissues, some observations have been at variance, notably those of Delarue, Linell and McKenzie.[4] They placed tantalum foil in the subarachnoid space over the traumatized cerebral cortex of dogs and reported thickening of the dura, encapsulation of the tantalum, thickening of the leptomeninges and adhesions to the traumatized cortex. Cone, Pudenz and Odom,[3] and Pudenz and Odom[6] found, on the other hand, that tantalum placed in the subdural space over the traumatized cerebral cortex of cats became encapsulated with a thin membrane, the inner layer of which was formed by the slightly thickened arachnoid. Robertson and Peacher[7] used tantalum foil over the traumatized cerebral cortex of human patients. At reexploration, they found that the tantalum had been encapsulated by a thin fibrous membrane, which was loosely adherent to the dura and to the arachnoid, but that no adhesions were present between the foil and the underlying cerebral cortex. Graf and Hamby[5] employed finely divided tantalum as a contrast medium for demonstration of sinuses resulting from intervertebral disc protrusions. In one of their patients reexploration was carried out. The only reaction found was the presence of a few multinucleated cells near the tantalum particles.

These reports have been selected because they indicate that certain physical forms of tantalum elicit a considerable response from the tissues about

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them. Numerous studies of reactions to tantalum in the form of large sheets and plates have uniformly indicated a minimal response of the tissues in which the tantalum had been placed.

It was felt that powder was the best physical form in which to study the effects of radioactive tantalum unless the tissue reaction to the tantalum particles themselves was confusing. The reason for preferring the powdered form was that this has a much greater surface area for a given weight of metal than has foil, plate or gauze.

MATERIALS AND METHODS

The tantalum powder was of three sizes: 120 mesh on 200 mesh, 300 mesh on 400 mesh, and air floated.* The powder was sterilized by autoclaving for 7 minutes at 27 lbs. pressure.

The experimental animals were cats weighing 2 to 4 kg. and monkeys (*Macaca mulatta*) weighing 2 to 4 kg. Anesthesia was accomplished by veterinary nembutal injected intraperitoneally in the cats and intravenously in the monkeys. In all, 24 cats and 55 monkeys were used.

The sites of implantation of the powdered tantalum were (1) the intracranial subdural space; (2) the basilar cisterns; (3) the cerebral hemispheres; (4) the lateral ventricles; and (5) the spinal subdural space in the lumbar region.

When the powdered tantalum was placed in the *intracranial subdural space*, a small frontal osteoplastic bone flap was made and the dura opened. Five-tenths gram of powder was then sprinkled on the exposed arachnoid. In the animals in which the powder was introduced into the *basilar cisterns*, a midline suboccipital exposure was secured, through which 0.5 gm. of the tantalum was placed in the cisterna magna. When the tantalum was to be implanted in the substance of the *cerebral hemispheres* or within the *lateral ventricles*, a frontoparietal craniotomy was carried out and a track made with a sucker into the white matter or lateral ventricle. Five-tenths gm. of the powder was then inserted by means of a small scoop. In the experiments on the reaction in the *lumbar subdural space*, a wide laminectomy was made from L1 to L5, the dura opened in the midline and 0.5 gm. of powder laid on the presenting spinal arachnoid.

All wounds were closed in layers with fine black silk, except in the cats of the intracerebral and intraventricular series; in these animals the dura was left open but the scalp was closed.

Roentgenograms were obtained on all animals postoperatively, as well as at the time of sacrifice. Sacrifice was effected by overdoses of intravenous nembutal. The brains and spinal cords were removed intact and fixed in 10 per cent formol-saline. Sections were stained with hematoxylin and eosin routinely and with phosphotungstic acid-hematoxylin when special study was indicated.

RESULTS

1. *Tantalum Powder in the Intracranial Subdural Space.* Twelve monkeys were used, of which four received 120 on 200 mesh, four 300 on 400 mesh.

* Supplied by the Ethicon Suture Laboratories of Johnson & Johnson Company, New Brunswick, N. J., to whom our thanks are due. The term "120 mesh on 200 mesh" means that the particles had passed a screen with 120 meshes to the square inch but had failed to pass a screen with 200 meshes per square inch. The particles of the "air floated" powder varied from 10 to 50μ in diameter.

and four air-floated powder. Three of the 12 animals died, 1 each on the 5th, 6th, and 17th days postoperatively. One death was due to diarrhea and the other 2 to injuries unrelated to the experimental procedure. The 9 surviving monkeys were sacrificed 30 days after operation. During the period of observation, no abnormalities of behavior were noted.

On *gross* examination, the tantalum was found to be adherent to the inner surface of the dura in all 9 monkeys. With the two coarser grades of powder the particles were enmeshed in delicate fibrous tissue, forming a compact mass which could be lifted from the underlying cerebral tissues. No meningocerebral adhesions were demonstrated (Fig. 1). The air-floated powder could be seen on gross inspection to have spread over an area 1.5 cm. in diameter. This was confirmed by the roentgenograms (Fig. 2), which also indicated that the powder had not spread to distant sites.

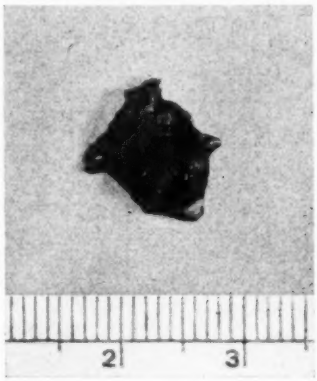

FIG. 1. Aggregate of 120 on 200 mesh powder in the cerebral subdural space. The powder is held together in a compact mass, which is not adherent to the leptomeninges.

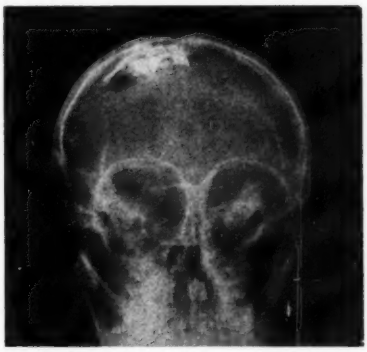

FIG. 2. Postmortem roentgenogram showing the extent to which air-floated tantalum powder spread when introduced into the cerebral subdural space.

On *microscopic* examination, the cerebral cortex beneath the discrete masses of the two coarser grades of powder was the site of slight compression atrophy, with mild increase in the number of astrocytes in the outer layers of the cerebral cortex. No inflammatory cellular infiltration was noted. In the monkeys receiving air-floated powder, the particles of tantalum were found to have passed through the arachnoid (Fig. 3). Many were lying free in the subarachnoid space but some of the smaller particles were found within phagocytes. The tantalum powder had entered the Virchow-Robin spaces, distending them but not penetrating the surrounding tissues or the lumina of the blood vessels (Fig. 3). Astrocytes were somewhat increased in the cerebral cortex beneath the areas where tantalum was found and near the Virchow-Robin spaces containing the powder. Sections of the brains at a distance from the operative site showed no evidence of further spread of the tantalum and there was no inflammatory reaction.

The spinal cord was examined in total length in 5 animals. Neither in the gross nor in microscopic examination at three levels was any abnormality found.

2. *Tantalum Powder in the Basilar Cisterns.* Five monkeys and 6 cats were used in this series and only the 300 on 400 mesh powder was implanted. Of the 5 monkeys, 2 died as the result of anesthetic accidents. One of the 3 surviving monkeys was sacrificed at 7 days and the other 2 at 21 days. Of the 6 cats, 1 died on the 3rd postoperative day, another on the 5th and a third on the 9th. Death in each of these cats was preceded by signs of intense

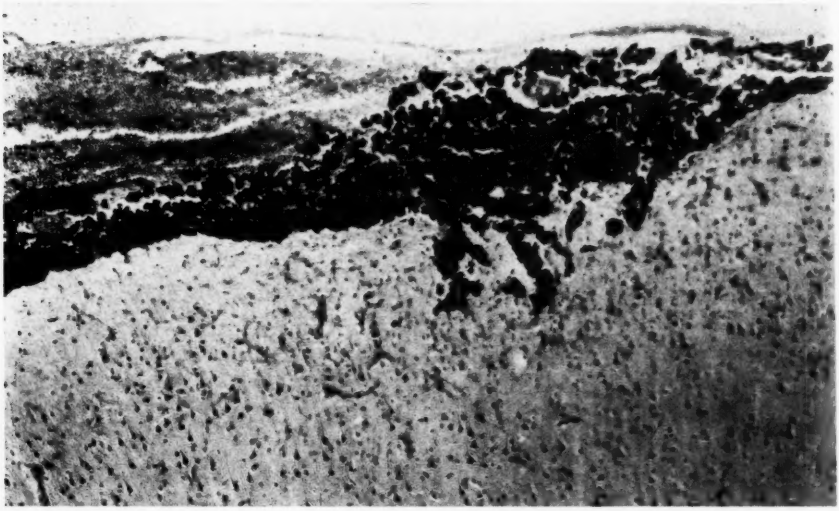

FIG. 3. Photomicrograph of the leptomeninges and underlying cerebral cortex in a region where air-floated tantalum powder had been introduced into the subdural space. Note the spread of the powder to the subarachnoid space and some of the Virchow-Robin spaces.

meningeal irritation. In the other 3 cats these signs did not develop and they remained healthy; 2 were sacrificed at 2 months and 1 at 3 months after operation.

As seen *grossly* at autopsy and as confirmed by roentgenograms, 3 of the 6 animals surviving to the time of sacrifice were found to have received the tantalum subdurally. The spread of the tantalum powder was confined to the field of operation in these animals. In the other 3 and in the 3 cats that died following the development of signs indicating meningeal irritation, the powder was found to have been placed within the cisterna magna. The tantalum in each of these animals was widely dispersed over the floor of the posterior fossa and downward along the cervical portion of the spinal cord. The material could be seen in masses of various sizes on both dorsal and ventral surfaces of the brain stem and cervical segments (Fig. 4). No tantalum was identified at lower levels of the spinal cord. In regions where the men-

inges were free from the powder, they were normal in appearance. Nowhere was there evidence of purulent exudate or of adhesions between the dura and arachnoid.

On *microscopic* examination, scattered particles of the powder were found somewhat more widely disseminated than was apparent on gross study. No tantalum, however, was found above the falx or in the thoracic and lower levels of the spinal cord. In those portions of the meninges containing only a few isolated powder granules, there was a moderate increase in the connective tissue of the arachnoid and the pia appeared thicker than usual. Lymphocytes were present in considerable numbers but no polymorphonuclear leucocytes were seen. There were no giant cells or evidence of phagocytosis of the tantalum. In regions of the meninges where there were groups and masses of powder granules, the histological picture was quite different. The tantalum particles were held together by collagenous tissue and between masses there were wide bands of connective tissue. Some of the smaller particles were within giant cells, though these were not a conspicuous feature. The pia, as such, could usually not be separated from the connective tissue, which was so abundant in the subarachnoid space. Lymphocytes were scattered through the region but were not numerous at any point. The surface of the arachnoid was smooth and intact in all regions. No changes were noted in the underlying brain and spinal cord tissue, even in the places where the meningeal reaction was most extensive.

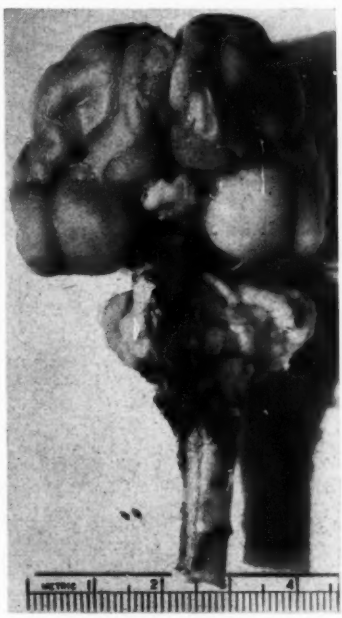

FIG. 4. Extent of spread of 300 on 400 mesh tantalum powder when introduced into the basilar cistern.

In the animals studied a few days after operation lymphocytes were more numerous and the fibrous tissue less dense and abundant than at 2 or 3 months. The differences at various time intervals were not great, however. No purulent meningitis was found in any of the animals.

3. *Tantalum Powder in the Cerebral Substance.* There were 7 monkeys and 4 cats in the series. In all the animals, air-floated powder was placed in the right frontal lobe. The monkeys were sacrificed at 4, 6 and 8 weeks, and the cats at 2 and 4 months.

On *gross* examination and in roentgenograms, the mass of tantalum powder remained discrete. In all animals, a firm, fibrous, meningocerebral scar was present at the site of the cortical incision. The superficial portion of the

cerebral wound was filled with dense tissue in which scattered particles of tantalum were seen. A mass of the powder was found in each instance at the bottom of the tract. It was judged that the meningocerebral scar and the dense tissue along the line of cortical incision were due to the operative procedure.

In *microscopic* sections, the powder was found as single grains or coalesced in compact masses (Fig. 5). When the tantalum remained in individual particles, it was largely phagocytosed in cells which were mostly compound granular corpuscles but in some instances giant cells appeared (Fig. 6).

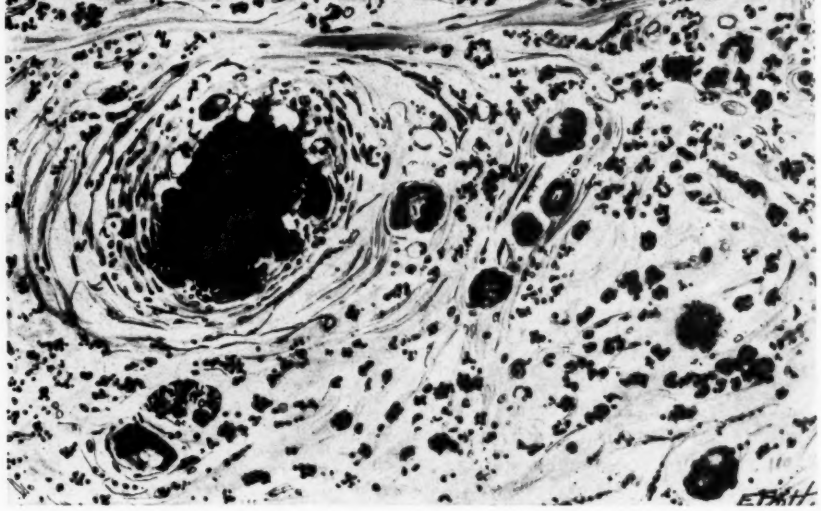

FIG. 5. Giant-cell formation and encapsulation of an aggregate of air-floated tantalum powder in the substance of a cerebral hemisphere. Camera lucida drawing, low power, phosphotungstic acid-hematoxylin stain.

Each phagocyte contained several grains of powder. These cells were scattered through loose-textured tissue rich in collagen fibers.

In the animals sacrificed at the longest intervals after operation, astrocytes became progressively more numerous. When the powder granules had coalesced, they were sometimes surrounded by fibrous tissue, often with giant cells at the border of the tantalum mass (Fig. 5). In other instances there was little or no reaction about masses of powder of the same size and apparent character. Considerable disruption of the cerebral substance was found for 1 to 2 mm. beyond the area in which the powder had been placed but at greater distances the brain appeared normal.

4. *Tantalum Powder in the Lateral Ventricle.* Four monkeys were used in this series. These were sacrificed at 3, 4 and 6 weeks after 0.5 gm. of 300 on 400 mesh powder was introduced into the lateral ventricle.

On *gross* examination, the condition of the meninges and brain at the operative site was similar to that found in the preceding series, the cortical incision being closed by dense tissue and covered by meningocerebral adhesions. On coronal sections, the ventricles were normal in size and the ependyma free from exudate and membrane. No shift in the position of the tantalum mass was detected by roentgenograms or by study of the brain grossly.

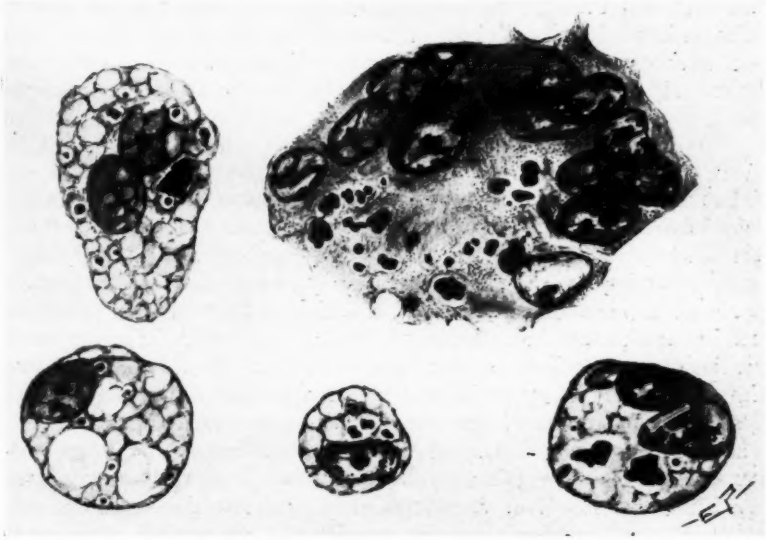

FIG. 6. Giant cells containing granules of air-floated tantalum powder in the substance of a cerebral hemisphere. Some of the cells also contain degenerated myelin. Camera lucida drawing ×1300, phosphotungstic acid-hematoxylin stain.

In *microscopic* sections, the surface ependymal cells were usually destroyed beneath the tantalum. The powder granules were loosely held to the cerebral tissue by very delicate collagen fibers, in the meshes of which were scattered compound granular corpuscles. New capillary formation was unusual. There was no giant-cell reaction. In the cerebral tissue just beneath the tantalum, a narrow zone was present in which fibroblasts were seen and in which the number of microglia and oligodendroglia was increased. No astrocytosis was noted. In 2 animals, powder was present beneath an intact layer of ependymal cells. About these tantalum granules, the infiltration of reactive cells was less extensive than it was about those lying on the exposed subependymal tissues.

5. *Tantalum Powder in the Spinal Subdural Space.* In the series, 0.5 gm. of 300 on 400 mesh powder was placed in the spinal subdural space of 3

cats. This was done through a total laminectomy at L1-L5. Two of the cats were normal postoperatively but in the third there developed transient weakness of the hind legs, which disappeared after 4 days. One cat was sacrificed 3 weeks and the other two 6 weeks after operation.

The entire spinal cord was removed at autopsy. *Gross* inspection showed that the tantalum powder was well localized on the dorsal surface of the spinal cord at the level of insertion. This was confirmed by roentgenograms. There was no spread either up or down the spinal cord. The leptomeninges were smooth and glistening, being free from adhesions and exudate.

On *microscopic* study, the tantalum was found to lie in the subdural space of each animal. In all portions of the leptomeninges, the arachnoid was intact. A somewhat increased number of lymphocytes was present in the subarachnoid space beneath the tantalum but no fibrous-tissue proliferation or giant-cell formation was noted.

DISCUSSION

The responses of the central nervous system to non-radioactive tantalum powder have been studied to determine the influence of the site in which the material was placed, of the size of the powder granules and of the length of survival after implantation. In order to secure information on the relative importance of these three experimental variables, three sizes of powder were placed in one site and then one size of powder was implanted in various locations. Animals of each series were allowed to survive for different lengths of time. Since this study was essentially designed as a control for work on radioactive tantalum now in progress, emphasis in selecting times of sacrifice was laid on long-time results, rather than those found within hours or days. In general, the tissue reaction was little different in animals surviving a few weeks from that in others sacrificed at several months, regardless of the location in which implantation was carried out or the size of the powder. For this reason, the histological changes found in the animals of each series have been described together.

The cerebral subdural space was chosen as the site for evaluating the influence of powder size. In the animals receiving the two coarser grades of powder, the particles of tantalum were held together in a compact mass (Fig. 1) which was adherent firmly to the dura but not to the arachnoid. The only changes in the underlying cerebral cortex were those due to compression. On the other hand, the granules of the finest powder (air-floated) penetrated the arachnoid into the subarachnoid space for some distance, even entering some of the Virchow-Robin spaces (Fig. 3). It did not extend, however, beyond the exposed cortex and was not found at the base of the brain or in the spinal subarachnoid space. That this difference was due to particle size and not to operative trauma is suggested by the facts that these findings were consistent in all the animals of the series and that great care was used to make the operative technique identical.

The size of the particles was not the only factor in determining whether

or not the tantalum would spread, as shown by examination of the animals in which the medium grade of powder was introduced into the basal cisterns. Although similar particles were held together in a firm mass when placed in the cerebral subdural space, the tantalum in the basal cisterns was found widely dispersed in the floor of the posterior fossa and in the subarachnoid space of the cervical spinal cord (Fig. 4). The particles caused a fatal meningeal reaction in 3 of the 9 animals. That these fatalities were not due to contamination was shown by the fact that no purulent exudate was present, even in the animals dying a short time after operation. In animals that survived, the connective-tissue proliferation was greater than that induced at any other meningeal site. The amount of connective tissue was directly correlated with the amount of tantalum in the area but was little, if any, greater in the animals allowed to survive several months than it was in those sacrificed a shorter time after implantation. Once the tantalum particles were encapsulated, there was no evidence of further overgrowth of connective tissue. Hydrocephalus was not present in any of the animals.

The excessive meningeal irritation, tissue reaction and powder migration caused by the tantalum in the cisterns was in striking contrast not only with the behavior of the tissues toward similar material in the subdural cerebral space but also in the spinal meninges, where tissue reaction and migration were absent or minimal. The fact that there was at least one region where the presence of the powder led to severe reaction and a considerable number of fatalities indicated the importance of selecting material in a form proved not to migrate freely if any clinical use of tantalum powder is contemplated.

There was no distant spread when tantalum powder was placed within the substance of the cerebral hemisphere or directly on the ependymal surface. In studying this material it was impossible fully to differentiate the effects of the operative procedure from those due to the tantalum. The phagocytosis of the powder was clearly not related to the operation but at least some of the proliferation of fibrous tissue and astrocytes was caused by the trauma incident to the insertion of the powder. This is confirmed by the density of the reaction in the upper portion of the cortical wound, where the only powder was a few grains which were spilled while the material was being placed at the bottom of the cortical incision, and the similarities between the cortical scars in the intracerebral and intraventricular series. The behavior of the tissues toward the tantalum depended to a considerable extent on whether the granules were separate or in aggregates. Similar effects under quite different conditions have been recorded elsewhere.[1] On the whole, it was judged that the reactions to tantalum powder within the cerebral tissues were considerable in the microscopic preparations but that they would not be of great clinical importance.

SUMMARY

The tissue reactions induced by non-radioactive tantalum powder were studied with regard to three variables: the size of the powder granules, the

site of implantation, and the length of survival after implantation.

When the granules were 10 to 50μ in diameter, they migrated for some distance in the subdural and subarachnoid spaces, even entering the Virchow-Robin spaces. Larger particles were held in place by fibrous tissue.

Severe reactions with fatalities were seen only when the material was introduced into the basal cisterns.

In the cerebral substance, individual particles were phagocytosed. About aggregates, a fibrous capsule was formed and giant cells were present.

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CASE REPORTS AND TECHNICAL NOTES

MYELOGRAPHIC DIAGNOSIS OF SACRAL PERINEURIAL CYST

Z. Edin Taheri, M.D., Paul Riemenschneider, M.D., and Arthur Ecker, M.D.
State University of New York, College of Medicine, and Syracuse Memorial Hospital, Syracuse, New York

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Sacral perineurial cyst has come to attention in recent years as a possible cause of symptoms referable to the cauda equina. The symptoms include lumbosciatic pain and urinary retention. In each case previously reported, no definite preoperative diagnosis could be made.

Myelography has been considered of no value in these cases because of the frequent lack of communication between the cyst and the subarachnoid space. However, in the case presented such communication was present and permitted preoperative visualization of the lesion. As far as we know, positive myelograms have not been reported previously in this condition.

CASE REPORT

The patient was a 38-year-old woman who had suffered low back pain intermittently for 15 years, but none for the past 3 years before the present episode. Two weeks prior to admission, she lifted a 50-pound tray and felt severe lumbar pain. Four weeks of bed rest produced no improvement. The pain began to radiate down the posterolateral aspect of the right lower limb and was increased by coughing or straining.

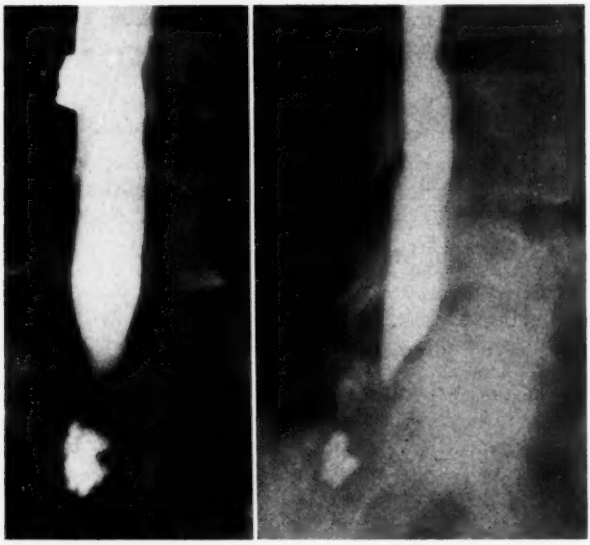
Examination. She was unable to bend forward or to walk on toes or heels. The patellar and Achilles reflexes were normal. There was no tenderness along the course of the sciatic nerves. Straight leg raising was permitted to 120° on the left and 80° on the right; when either leg was lifted, pain was referred to the right lumbosacral area. Sensory status was normal. Vertebral tenderness was limited to the spinous process of the 5th lumbar vertebra. There was slight atrophy of calf and thigh muscles on the right side. Plain x-ray films of the lumbosacral region were normal.

Myelography. Under the fluoroscope a small amount of pantopaque passed from the terminal portion of the sac to a small irregular diverticulum just caudal to the sac. The opaque medium did not return to the main portion of the sac after the patient was tilted back. On the basis of this finding, together with confirmatory spot films (Figs. 1 and 2), a diagnosis of sacral perineurial cyst was made.

Operation, Feb. 21, 1951. There was no ruptured disc at the lumbosacral space, but far laterally there was bulging of the disc in the region of the posterior ganglion of the right 1st sacral nerve. The sacrum was unroofed and the lower end of the dural sac was found to have numerous tiny outpouchings. There was a large perineurial cyst on the right which measured 5×7×3 mm. (Fig. 3). Tantalum clips were placed above and below the cyst. The cyst and adjacent portion of the right 2nd sacral nerve were removed. There was a similar cyst, 3×3×5 mm., on the left 2nd sacral root.

Postoperative Course. The patient was completely free of pain and other symptoms. No sensory loss could be demonstrated and the rest of the neurological examination was negative. Postoperative myelograms demonstrated the small cyst on the left with its narrow pedicle from the dural sac.

The patient returned to her work as factory inspector 5 months after operation and when last heard from, 7 months postoperatively, felt entirely well.



FIGS. 1 and 2. Preoperative myelograms. (*Left*) Anteroposterior view, showing pantopaque which is trapped in the cyst. The lowest part of the dural sac extended to the top of the cyst as determined by other films made with patient erect. (*Right*) Lateral view.

Microscopic section of the specimen showed sensory and motor roots; no cyst wall was visualized. There was moderate axonal degeneration of the motor and sensory roots.

DISCUSSION

Attention was called to the presence of these cysts in the posterior spinal nerve roots, within the perineurial space, by Tarlov.[4] He found 5 instances of cysts attached to the posterior sacral and coccygeal nerves in a study of the filum terminale in 30 autopsies, without any correlated clinical signs and symptoms during life.

FIG. 3. Operative view of lower end of the dural sac, showing perineurial cyst on right, before its removal.

In 1948, Tarlov[5] reported a case of lumbosciatic pain due to a perineurial cyst, which was removed with abolition of symptoms. Weiford[6] reported a patient with urinary retention due to a perineurial cyst who was operated on successfully.

These cysts are not parasitic or neoplastic. The cyst develops in the space between the endoneurial and the perineurial sheath (perineurial space). It may arise from arachnoidal proliferation.[2] A possible origin of the cyst from a congenital diverticulum of the dura mater or a herniation of the arachnoid through a congenital defect of dura has been suggested by Elsberg, Dyke and Brewer.[1] Schreiber[3] has suggested a traumatic origin for some of these cysts. As our case shows, the connec-

tion with the spinal subarachnoid space may be patent and permit myelographic visualization.

SUMMARY

There is reported a case of multiple sacral perineurial cysts in which myelography permitted preoperative diagnosis.

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PYOGENIC SUBDURAL ABSCESS OF THE SPINAL MENINGES

REPORT OF TWO CASES

Juan Negrin, Jr., M.D., and Robert A. Clark, Jr., M.D.*
Neurosurgical Service, Bellevue Hospital (Cornell, Second Surgical Division), New York, New York

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Acute suppuration of the coverings of the spinal cord, aside from leptomeningitis, is an uncommonly encountered condition. The literature now contains more than 200 cases of spinal epidural sepsis;[10] localized subdural collections of pus have rarely been recorded. Because of its infrequent occurrence, it would seem worth while to present the case reports of two patients with pyogenic subdural abscesses recently treated on the Cornell Neurosurgical Service at Bellevue Hospital.

CASE REPORTS

Case 1. L.S., a 66-year-old Hebrew widow of Russian birth, was admitted to a medical service on Feb. 14, 1949 complaining of twitchings of the arms for 2 days. She had had diabetes of mild degree for 12 years. Despite the lack of careful control, she had been in apparent good health until 6 weeks before admission, when a furuncle developed on the anterior abdominal wall in the right lower quadrant. About 1 week later, she began to have rather vague pains in the neck, head, chest, abdomen, and extremities. She felt ill and began to eat less and drink large quantities of water. During this period, she noted fine tremulous movements of the hands, and on the day of admission, she experienced a seizure characterized by outcry before and during the attack, extensor rigidity of the upper limbs with carpal spasm, tight closure of the eyes, and questionable conjugate deviation of the eyes up and out to the left. There were no clonic movements, no impairment of consciousness, little if any involvement of the lower

* Resident in Neurological Surgery.

limbs, and no incontinence. Each episode lasted 20–30 seconds. They were said to have been stopped for a time by the administration of intravenous calcium gluconate.

Examination. The patient was an obese, elderly female who was apprehensive, noisy and uncooperative. No abnormal neurological signs were recorded.

She had albuminuria, glycosuria, a trace of acetonuria, and hypercalcemia. WBC was 31,150 mm^3, with 90 per cent polymorphonuclear leukocytes. Blood urea nitrogen was 29 mg. per cent. Lumbar puncture yielded clear, xanthochromic fluid under an initial pressure of 120 mm. of water; protein was 432 mg. per cent; WBC was 270 with 30 per cent polymorphonuclear leukocytes and 70 per cent lymphocytes. Culture of this fluid grew Streptococcus viridans.

Course. On the 2nd hospital day she began to have marked nuchal rigidity. On the 5th day she claimed that she could no longer move her lower limbs. She was at times opisthotonic and coarse, irregular clonic movements of the lower limbs were beginning to develop. Sulamyd 1 gm. 4 times a day and penicillin 200,000 U every 3 hours were begun, the culture of the first CSF being reported at this time.

On the 8th day, there was flaccid quadriplegia with bursts of extensor spasms in all limbs. The neck was quite rigid. The patient was alert and oriented, all head functions were intact, and she complained of pain in the postcervical region. On lumbar puncture, the fluid was cloudy and xanthochromic, and it clotted. It contained 18,000 WBC, 98 per cent of which were polymorphonuclear leukocytes. Manometric readings demonstrated an almost complete block. Cisternal tap yielded fluid which was much clearer and contained only 1,000 WBC. One cc. of pantopaque was placed in the cisterna magna and was seen to stop at the upper level of C3.

At this time, the impression was that the patient had an epidural or subdural abscess, the latter being strongly suggested by the unusually high number of WBC in the CSF.

Operation. Complete laminectomy of C3-6 was done under endotracheal anesthesia. The laminae seemed more friable than normal, and the rongeured edges oozed freely. The exposed dura was tense and nonpulsating, the epidural space being free of any abnormal material. The dura was nicked and approximately 1 cc. of thick, greenish-yellow pus escaped. Culture of this material grew Staphylococcus aureus, coagulase positive. The dura was opened longitudinally for the entire extent of the exposure. More pus escaped, and it was seen to be coming from anteriorly as well. The sudural space was irrigated with copious amounts of normal saline through a #12 F. catheter. This was passed up and down over the cord in the subdural spaces for 5–6 cm. both anteriorly and posteriorly, with more purulent coagula being washed out from about 2–3 cm. caudally. At the end of this procedure, the arachnoid membrane was intact, and the cord pulsated nicely. The dura was left open for about 1 cm. inferiorly and a fine rubber catheter was placed down to the epidural space and brought out through the inferior angle of the wound. The incision was closed in layers using chromic catgut for the buried sutures and silk for the skin.

Postoperative Course. The extensor spasms of the lower limbs ceased by the 2nd postoperative day, but there was no adequate response to intensive measures, and on the 55th postoperative day the patient expired with large deep decubiti. Permission for autopsy was not granted.

Comment. In this case, the subdural localization was suspected preoperatively because of the high number of white cells found in the spinal fluid, the cellular reaction in the usual epidural abscess being much lower.[10] This would seem to have been a logical assumption, since the infection is intimately surrounding the arachnoid membrane and should, therefore, cause a greater pleocytosis in the subarachnoid fluid than an epidural collection of pus. However, the only three analogous cases previously reported, which gave the number of cells in the cerebrospinal fluid, do not bear this out as a differential point.[1,3,5] In addition, in our case Streptococcus viridans was cultured in the spinal fluid while the subdural pus grew Staphylococcus

aureus, suggesting that the patient might have had a concomitant leptomeningitis due to an entirely different organism from that found in the subdural space. From comparison of the clinical course of subdural abscess with that of epidural abscess, there does not seem to be any reliable differential point to distinguish the two. Subdural abscesses are and will be encountered with the diagnosis unsuspected preoperatively.

In operating on patients suspected of having epidural abscess, if nothing is found in the epidural space, it is felt that one should not hesitate to open the dura in search of subdural purulence. The following case serves to emphasize the point that such diseases are true neurosurgical emergencies.

Case 2. R.D., a 51-year-old negro male, was admitted to a medical service on Jan. 1, 1950. Aside from pins-and-needles sensation in the extremities and occasional shooting pains in the lower limbs, he had been free of neurological complaints until about 3–4 weeks before admission, when there developed difficulty in walking, which forced him to watch his feet to keep from stumbling. This was accompanied by some weakness of the lower extremities. These symptoms progressed until the patient was unable to walk or stand without support. At the same time, he had chills and fever, anorexia, and low back pain, particularly on the left side. For the last 5 days he had been obstipated. Six weeks previously, he had entered a surgical service with a hand infection; at that time, a lumbar puncture was done because of physical signs of tabes dorsalis.

Examination. He was an emaciated negro, whose findings, aside from those related to tabes dorsalis, were paresis of the left lower limb and a sensory level to pin prick on the left side to the umbilicus.

Urine was normal save for a trace of albumin. Hb. 10.7 gm. per cent, WBC 31,500/mm.^{3} with 96 per cent polymorphonuclear leukocytes. Blood urea nitrogen 23 mg. per cent. Blood Mazzini 4+. X-rays of lumbar spine revealed 6 lumbar vertebrae and scoliosis. T. was 102.6°F.

Course. The patient was started on penicillin, 500,000 U twice a day. The temperature rose at first to 104°F. but later decreased by lysis.

Repeated lumbar punctures during the first 5 days yielded purulent material which grew out diptheroids and Streptococcus hemolyticus.

On the 5th hospital day, a cisternal puncture was performed; the fluid was clear and colorless, with 9 lymphocytes, negative Pandy, and a 4+ Wassermann. One cc. of pantopaque was instilled into the cisterna magna and allowed to descend over the cord; no block was observed. Lumbar puncture was repeated on the following day, and just as the dura was pierced 2–3 cc. of pus were obtained. The patient was therefore taken to the operating room.

Operation. L3-5 laminectomy was performed. The ligamentum flavum was thickened and intimately adherent to the dura; there was no epidural fat and no pulsation of the dura. When the dura was opened, purulent material gushed forth; this proved to be sterile on culture. At the level of L5 an abscess wall was found incorporating the lower roots of the cauda equina. This extended in the cul-de-sac of the dura. After irrigating the subdural space both proximally and distally with 1:1000 penicillin solution, a #12 F. catheter was passed in both directions in the subdural space and fixed in place by loosely approximating the very friable dura. The wound was then closed in layers using chromic catgut for the buried sutures and silk for the skin. A Penrose drain was placed down to the epidural space and brought out through the inferior end of the incision.

Postoperative Course. This was exceptionally smooth, but recovery was gradual and slow. By the 82nd hospital day the patient was ambulatory with the aid of a cane. His urinary retention, present since the 2nd hospital day, cleared and his residual urine was only 50 cc.

Comment. The diagnosis was suspected when pus was obtained by lumbar puncture immediately after piercing the dura, in the absence of a leptomeningitis. This was confirmed at operation.

DISCUSSION

The pathogenesis in Case 1 was felt to be a subdural localization of bacteria secondary to a bacteremia during the period of the anterior abdominal wall infection. A similar case was reported by Bennett and Keegan[3] in 1927, and it is the only one in which there was a recovery. The patient was a 32-year-old male who had osteomyelitis of the ilium 6 years before the onset of a paraplegia, which developed within 1 month. The preoperative diagnosis was epidural abscess, but at operation pus and granulation tissue were found in the subdural space exclusively, at the level of the D4 vertebra.

In 1936 Chi[5] reported the case of a 48-year-old Chinese soldier who had paraparesis approximately 3 weeks after the onset of acute low back pain; this was diagnosed as sacro-iliac arthritis, and the patient improved on bed rest. Just before his discharge from the hospital several boils appeared in the right flank from which Staphylococcus aureus was cultured. Two weeks later he had paralysis of one lower limb and marked weakness of the other. The spinal fluid in this case contained only 48 white cells. At operation pus and granulation tissue, encountered subdurally at the level of D9 vertebra, were removed. There was no neurological improvement, and the patient died 16 days after operation.

A third case was recorded by Abbott[1] in 1940. The onset of the paralysis was more gradual than in our Case 1. At autopsy a subdural collection of purulent material was found in the upper lumbar and lower dorsal regions. There was also a leptomeningitis, which the author interpreted as being secondary to the subdural abscess.

In 1945 Freedman and Alpers[8] reported 2 cases, in both of which postmortem examination was made. In one, an abscess of the right arm developed, requiring surgical drainage; during the acute phase the patient was said to have had a bacteremia. Several weeks later he was hospitalized because of clinical signs of pulmonary infection, followed by pain in the back. He was febrile, and there developed nuchal rigidity, reflex, sensory and motor power changes in the left leg, radicular pain in the lower limbs, and urinary retention. Lumbar puncture revealed an almost complete block with a high spinal fluid protein and pleocytosis of 4 and 1600 white cells on two separate taps done 2 days apart. A laminectomy from T11-L1 was done 3 weeks after admission. The dura did not pulsate and was greatly thickened. On opening the dura pus was encountered; this grew out Staphylococcus aureus. The patient died on the 1st postoperative day. At postmortem examination, pus and granulation tissue were found in the subdural space over the entire cord. The other case was that of a middle-aged diabetic female who entered the hospital because of the development of pneumonia 2 months before with pleural effusion, and subsequent pain in her back. She was febrile and completely paraplegic. It was felt inadvisable to risk operation and 5 months after entrance she died of hypostatic pneumonia and multiple decubitus ulcers. In both of these cases the macroscopic and microscopic findings were limitation of the inflammatory process to the subdural space and changes in the cord attributed to interference with its circulation. The authors concluded that here too, as in epidural abscesses, the damage done to the cord was caused by alteration of the circulation of the cord rather than by compression.

It should be emphasized that in our Case 1 and in the previously reported cases cited above the infections were limited to the subdural space and were not extensions from the epidural space. Instances of the latter type of infections are also known to occur.[7,9,14,15]

It has been thought by some that epidural infections are invariably secondary to osteomyelitis of the vertebrae. That such is the case when the subdural space alone is infected is open to question. The lymphatic and venous drainage of the cord and its coverings is centrifugal; one would expect an infection from bone that by-passes the epidural space, as in cranial subdural empyema, to spread via a lymphatic or venous route; but the lymphatic and venous drainage of the cord is in the opposite direction for such a mechanism. It is believed, therefore, that no such primary osteomyelitic process in the vertebrae is a necessary fore-runner of subdural abscess of the spinal meninges. On the other hand, subdural empyema of the cranial cavity is known to be invariably secondary to infected paranasal sinuses, more particularly the frontal sinuses, or, less commonly, the mastoid air cells.[6] The venous and lymphatic drainage under normal conditions of intracranial pressure relations is from the skull centripetally to the great venous sinuses within the skull, as well as centrifugally. This, then, could explain how infection can pass to the subdural space from bone without being a direct extension from the epidural space.[6] It is also perhaps a reason for the relatively greater frequency of subdural empyema of the cranial meninges as compared to the analogous infection of the spinal meninges. Of interest is the fact that only 1 case of metastatic abscess of the cranial subdural space has been reported.[11]

In our Case 2 the abscess was felt to be the result of contamination of the lumbar subdural space at the time of the spinal tap 6 weeks before. It is similar to the case of Peacher and Robertson,[13] in which caudal anesthesia for delivery was followed by a lumbar subdural abscess. Their localization was based on the insertion of a spinal needle in the lumbar region and the obtaining of pus just as the needle pierced a momentary resistance, a sensation usually ascribed to entering the dura; the exact site was not confirmed surgically, as treatment consisted of instillation of penicillin through the spinal needle. In our Case 2 the diagnosis was made in the same way, and the localization was confirmed at operation. It likewise would seem to bear a close similarity to the case of Peacher and Robertson in its etiology. Arnett[2] reported another subdural abscess in the lumbar region after repeated spinal taps during the course of a meningitis. He also mentioned a similar case of Osler[12] in 1899.

Heusner,[10] in a footnote in his article on epidural abscesses, stated that he did not include a few subdural abscesses treated by his group. One wonders if the condition is not more common that the number in the literature would indicate.

Though this paper is concerned exclusively with pyogenic infections of the spinal subdural space, it should be mentioned that granulomatous lesions also occur in tuberculous, syphilitic, coccidioidal, and torula infections[4] as well as those due to contamination of the subdural space via dermal sinuses.[16]

SUMMARY AND CONCLUSIONS

Two case of subdural abscess are reported in detail, and the literature is reviewed.

These infections appear to be (1) secondary to a bacteremia or (2) caused by direct contamination of the subdural space with a spinal or caudal needle. In all of those secondary to bacteremia the pathogenic organism was Staphylococcus aureus.

The group that is metastatic overlies the cord, at least in part, and has had a uniformly bad prognosis; the pathologic changes in the cord seem to have been caused by interference with the blood supply rather than by compression. Those that are the result of direct contamination of the subdural space with a needle have

overlain the cauda equina, have had a better prognosis, and have presumably caused their neurological signs by compression.

In the former group, no differential point is found that might distinguish a subdural from an epidural abscess; its presence can only be suspected preoperatively. In the latter, it appears that the diagnosis can be made by careful lumbar puncture.

In both instances treatment should be an emergency laminectomy and drainage of the purulent subdural contents.

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TANTALUM CRANIOPLASTY AND REPEATED TRAUMA

Oscar A. Turner, M.D.*

Department of Neurological Surgery, Youngstown Hospital Association, Youngstown, Ohio

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There is uniform agreement that protection from trauma constitutes one of the major indications for cranioplasty. The necessity for such protection is greatest in the younger age group and increases with the size of the cranial defect.

Tantalum is probably the most commonly employed alloplastic material used for this purpose and while generally the thickness of plate employed has been sufficient to withstand considerable direct trauma, there has been some recent tendency to

* 2204 Glenwood Avenue, Youngstown 11, Ohio

use thinner sheets because of the facility with which the prosthesis may be formed to correspond to the contour of the skull. Weiford and Gardner,[5] in a recent review of 106 cases of tantalum cranioplasty, indicated that the thickness of the sheets employed had been reduced in successive stages from 0.020 to 0.007 inch and felt that the latter was of sufficient strength, was more easily and more accurately fashioned, and was less expensive. Gardner[1] noted that with tantalum sheet of 0.007 inch thickness, pneumoencephalography and arteriography could be done with adequate visualization of the air-filled ventricles or of diodrast-filled vessels.

Deformity of a tantalum implant due to trauma probably occurs more often than one would suspect from the infrequency with which it is mentioned in the literature. Lane and Webster[3] in 1947 mentioned the necessity for removal of a tantalum implant because of an abscess of the scalp after a blow at the site of a cranioplasty 11 months after the procedure had been done for a gunshot wound. In a recent review by Reeves,[4] no mention is made of this complication.

The following instance of gross deformity of a tantalum implant due to repeated trauma served to stimulate observations relative to the ability of various sizes and various thicknesses of tantalum plate to withstand direct trauma.

CASE REPORT

The patient was an 8-year-old boy, first seen on April 11, 1950, because of a compounded and comminuted fracture of the frontal region sustained when he was struck by an iron pipe. The fracture overlay the anterior portion of the superior longitudinal sinus and indriven bone fragments could be visualized radiologically at a depth of 2 cm. The comminuted area measured about 5.5. cm. in width with the central portion of the depression at the midline. The patient was in mild shock but there was no evidence of extensive intracranial damage.

Operative debridement was carried out and a 6 to 7 cm. tantalum plate of 0.007 inch thickness was used to cover the defect in the bone. No attempt was made to inlay the plate, which was fixed in position with several tantalum wedges driven through the outer table of the skull into the diploic space. The wound healed well and the patient was discharged from the hospital with no evidence of residual neurologic defect.

The patient was seen on July 15, 1950, because of a deformity of the scalp at the site of the tantalum implant. On July 4, 1950, almost 3 months after discharge from the hospital, he had been struck in the frontal region by a steel helmet of the type worn by steel workers. The patient had not been unconscious from the blow and had no complaint other than some tenderness at the site of the injury. Examination revealed a $3\frac{1}{2}$ cm. long depression of 6 to 7 mm. depth at the site of the cranioplasty. There were no neurologic abnormalities. Because the depression was not marked and in the absence of any apparent neurologic disturbance, replacement of the implant was deferred.

He was not seen again until June 1951, about 1 year after the first injury that had resulted in deformity of the tantalum plate. At this time there was a more marked deformity at the site of the implant and he gave a history that about 3 to 4 weeks previously he had been struck in the frontal region with a baseball. The distortion was more marked and the entire implant appeared to have been badly depressed. On June 16, 1951, the implant was removed (Fig. 1) and replaced with another of 0.015 inch thickness. At operation there was no evidence of damage to the local tissue as a result of the repeated trauma.

Observations were made on the ability of formed tantalum plates to withstand direct impact, using implants of approximately 2, 3, and 4 inch diameter and 0.005, 0.007, 0.010 and 0.015 inch thickness. All plates had the same relative contour and had been hand-formed on the anvil described in a previous communication. Figures were obtained by allowing a quarter-pound weight to drop from a specified height onto the plate, which was fixed in a manner similar to that used in a tantalum cranio-

FIG. 1. Convex surface of tantalum implant (0.007 inch thickness) removed from frontal region following repeated trauma.

plasty. The striking surface was a 1 inch square of aluminum bar and figures were obtained for the minimum impact, measured in inch-pounds, that would cause a definite indentation or distortion of the surface of the plate.

Table 1 gives a summary of the results obtained and it is of interest that the diameter of the implant made relatively little difference in the ability of the metal to withstand the impact. From the figures obtained, it became apparent that tantalum, even of 0.015 inch thickness, falls far short of the ability of the skull to withstand direct trauma. However, the fact that the implant does deform under direct impact may be a factor of safety in allowing dissipation of energy which might otherwise produce serious intracranial damage. The figures obtained suggest that tantalum of 0.010 inch thickness or less is not sufficient to withstand even very slight trauma without marked deformity and should probably be considered as unsuitable for cranioplasty except in very small defects or where considerable molding or contouring is necessary, as in the repair of defects involving the supraorbital ridge or orbital roof.

TABLE 1

Maximum energy requirements in inch-pounds necessary to deform tantalum plates

Thickness of Plate (inches)	Size of Plate (Diameter)		
	2 inch	3 inch	4 inch
0.005	0.75	1.0	1.0
0.007	2.0	2.0	2.0
0.010	2.5	3.5	3.5
0.015	5.0	4.5	5.5

ADDENDUM

Since the above was submitted for publication an additional instance of traumatic deformity of a tantalum implant has been observed. This was in a 14-year-old girl who struck her head against the corner of a sofa denting a 0.007 inch thick, $3\frac{1}{2}$ inch implant which had been used to cover a defect, after removal of an area of fibrous dysplasia of bone in the parietal area.

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THE LUCITE CALVARIUM

A CASE REPORT*

LT. COMDR. GALE CLARK (MC), U.S.N.†

(Received for publication September 5, 1951)

The purpose of this report is to describe a situation which was benefited by the use of a lucite calvarium. This is probably the first use of the acrylic cap in a human where there was avulsion of the scalp, skull, dura and brain; it was applied in an effort to get the patient into such condition that he could be evacuated to a "rear" area from the "forward" area at Wonsan, Korea.

The original work with the lucite calvarium, in a manner similar to that to be described, was done on monkeys by Shelden, Pudenz, Restarski and Craig[1,3] at the Naval Medical Research Institute at Bethesda, Maryland in 1943 and 1944. Acrylic substitutions for ordinary skull defects have been in use since 1940, and have recently been appraised in Reeves'[2] monograph on cranioplasty.

CASE REPORT

On Oct. 31, 1950 a right-handed hospital corpsman was involved in an accident when he was helping at the loading of a stretcher-patient onto a helicopter. He had evidently backed up toward the rear of the plane and was struck in the head by the whirling propeller, which rotates vertically. Three of the four blades of this propeller were broken off as they cut into his head.

The patient was rendered unconscious immediately and a battle dressing was applied to the macerated right side of his head. He was given last rites by the Catholic Chaplain and was transported to the hospital ship U.S.S. *Consolation* (AH-15) where he was admitted to the neurosurgical service in critical condition. He arrived aboard 60 minutes after the accident. Therapy for shock was instituted and plasma, blood, and intravenous fluids were given; his B.P. rose from 76/50 to 100/70.

Operation. Preparations were then made for craniotomy; however, because he was rapidly losing considerable amounts of blood and going into shock again, it was necessary to remove the head dressing and put hemostats on the bleeding pulsating arteries. Thus the exposed right middle meningeal and ascending parietal and parietotemporal branches of the middle cerebral artery were clamped (Fig. 1). Then the wound was packed with gauze; his head was shaved; and surgical "prep" was accomplished.

A large amount of foreign material including sand, flecks of paint from the plane's propeller, free chunks of scalp, pieces of skull bone, and blood-matted hair were removed from the cranial vault. Debridement was continued, using a sucker, and necrotic and macerated brain tissue was removed from the whole area of the parietal lobe, the posterior aspect of the frontal lobe, the superior half of the temporal lobe and the anterior part of the occipital lobe on the right. The white matter was involved to a depth of 5–6 cm. in certain areas and the temporal horn of the right lateral ventricle communicated with the wound. Hemostasis was

* The opinions or conclusions in this report are those of the author. They are not to be construed as necessarily reflecting the views or the endorsement of the Navy Department.

† 4345 Whittle Ave., Oakland, California.

difficult, especially with the stump of the middle meningeal artery and with the large branche of the middle cerebral artery. The edges of the skull defect were rongeured back until health dura was exposed all around the brain defect. Dr. J. Witt removed a large piece of fasci lata from the patient's right thigh and it was sutured in place across the dural defect, whic was the size of the palm of the operator's hand. As many of the attached scalp fragments a could be salvaged were put into their anatomical position and sutured with a plastic technique Large areas of scalp and skull substance were missing, and because the wound was not con sidered clean no primary scalp substitution was attempted. Ten cc. of saline containing 10,000

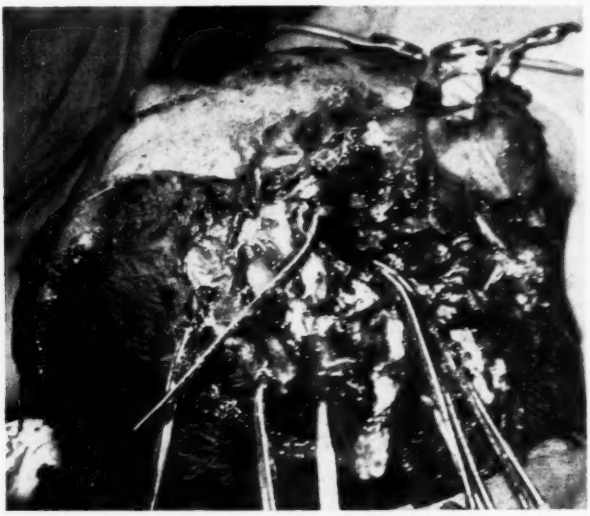

FIG 1 Day of injury. Face is to the left—occiput to the right. Hemostat angling toward 7 o'clock is on right middle meningeal artery.

units of penicillin were injected under the fascial transplant; the wound was dressed; and the patient was returned to the ward in fair condition.

Course. He regained consciousness in about 1½ hours after operation and was extremely irritable and noisy in spite of intramuscular paraldehyde and sodium phenobarbital. Chemotherapy for infection consisted of intrathecal penicillin, intravenous sodium sulfadiazine, and intramuscular penicillin and streptomycin.

On the 5th postoperative day the patient began to talk coherently but a CSF leak at the margin of the dural transplant became definite, and it was necessary to resuture the fascia lata flap.

On the 8th postoperative day a second CSF leak developed as another corner of the dural transplant broke down, necessitating a second repair. The fascial transplant appeared to be steadily shrinking and drying out and it ultimately separated from the dural edge a third time.

On the 11th postoperative day a vinylite sheet was sutured across the scalp wound to enclose a fluid media of saline containing penicillin over the exterior surface of the fascial flap. However, this provoked a markedly accelerated outpouring of leucocytes from the dura and scalp and it had to be removed in 48 hours.

On the 14th postoperative day Capt. F. E. Jeffreys, Dental Corps, U.S.N. fitted a mold jacket around the skull defect and an exact alginate hydrocolloid impression was made. From this mold a methyl ethyl methacrylate clear plastic calvarium was fashioned to fit exactly

all around the skull defect and maintain a water-tight integrity. Four holes were made for short vitallium bolts in the central area of the plastic calvarium (Fig. 2).

On the 16th postoperative day the fascial flap, which had broken down again, was removed and discarded. The brain wound was suctioned clean and irrigated; hemostasis was good. Then the lucite calvarium was fitted into place and fastened to the skull with wire (Fig. 3). Thus there was no scalp, no skull bone, no dura, and no brain tissue for a depth of 1.5 cm. in a large area; and there remained only the lucite calvarium between the white matter of the right side of his brain and the exterior.

Postoperatively he improved rapidly and hyperthermias (previously frequent and difficult to manage with alcohol spongings and ice water enemas) became rare and were easily

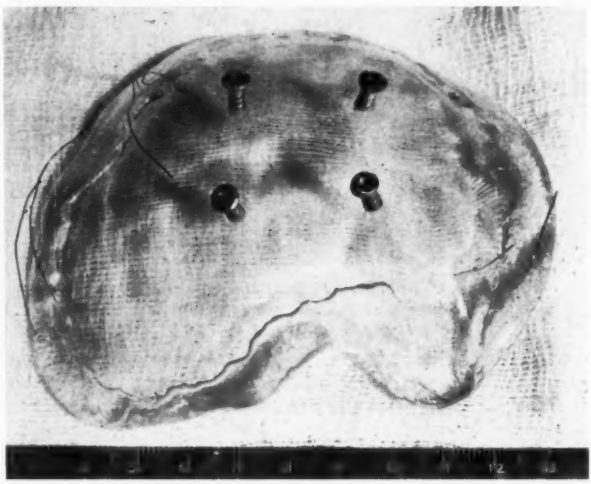

FIG. 2. Lucite calvarium. Outer lip is thinner than central area. Inner line conforms exactly with skull defect. Vitallium bolts may be removed under sterile technique from threaded holes. Wires at outer margin are for fixing cap to skull.

controlled. The lucite calvarium was not quite water-proof at one corner but the application of soft nonabsorbable bone-wax at the edge of the cap rendered it water-tight. Daily irrigations of his brain wound with saline and instillations of 10 cc. of dilute penicillin solution were carried out by unscrewing one of the vitallium bolts and injecting through its threaded opening.

This successful application of a clear transparent lucite calvarium offered opportunity for the study of brain repair, motion of the injured brain, chemistry and histology of the cerebrospinal fluid in repair, electroencephalographic correlations and numerous other studies.

Neurologic examination on the 27th postoperative day revealed the following positive findings. His mental attitude was interesting because he had been an operating-room technician previously and he recounted the story of the one time when he had scrubbed for a craniotomy—"The fellow had convulsions—he was operated on all right—but he died." He was able to write his name and serial number. He had a left homonymous hemianopsia but could see and recognize old friends. He was able to converse about recent events up to the day of his accident. There was no nystagmus and ocular movements were normal in all directions. Both pupils reacted to light, but consensual and convergence reflexes were bilaterally weak. Sense of hearing was markedly decreased on the right, but present; hearing was normal on the left. Sense of smell was impaired but coffee was pleasant and oil of clove and vinegar were unpleasant. Sense of taste was good and he could identify salt, sweet and bitter. His speech was

FIG. 3. Sixteen days after injury. Clear lucite calvarium about to be applied. Healing scalp, skull edges, dural margin and concave wound in brain seen.

slurring or scanning or explosive at intervals. He could swear and use a simple vocabulary with ease but was unable to perform any of the usual "tongue twisting" tests. There was flaccid paralysis of his whole left side and he was unable to walk although he could sit up in a wheel-chair. There was hyperreflexia on the left with clonus at the ankle. Babinski and

FIG. 4. 27 days after injury. Lucite cap in position. The whole concavity of brain wound is visible

confirmatories were pathologic on the left. Sensation on the left was affected with epicritic sensations absent, but protopathic sensations of deep pain from hypodermic needles and severe pinch appreciated but not localized. He had undergone a marked loss in weight.

The large deep concave brain wound remained clearly visible through the lucite cap for 6 weeks (Fig. 4). At the end of this period granulation tissue had grown across the wound from the dural edges and deep observation was terminated. The water-tight integrity of the cap to the skull was inadequate at intervals and necessitated frequent additions of bone-wax to the rim of the plastic cap in spite of its being held by three tightened wire loops.

The patient was transferred to the Naval Hospital in Yokosuka, Japan and then promptly transported to the United States, where he entered the U. S. Naval Hospital at Oakland on Jan. 2, 1951 for further treatment and disposition. There on Jan. 13, 1951 he expired with an uncontrollable cerebritis. He had survived 74 days after his injury.

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1 Pudenz, R. H., and Shelden, C. H. The lucite calvarium—a method for direct observation of the brain. II. Cranial trauma and brain movement. *J. Neurosurg.*, 1946, *3:* 487–505.

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3 Shelden, C. H., Pudenz, R. H., Restarski, J. S., and Craig, W. McK. The lucite calvarium—a method for direct observation of the brain. I. The surgical and lucite processing techniques. *J. Neurosurg.*, 1944, *1:* 67–75.

A SIMPLE RADIO-OPAQUE SCREEN FOR ANGIOGRAPHY

Gordon L. Smiley, M.D.*

Department of Surgery, Division of Neurosurgery, State University of Iowa, Iowa City

(Received for publication June 29, 1951)

A simple, flexible, leaded-rubber screen has been devised which reduces exposure to secondary or scatter radiation during angiography (Fig. 1). The 20-inch-

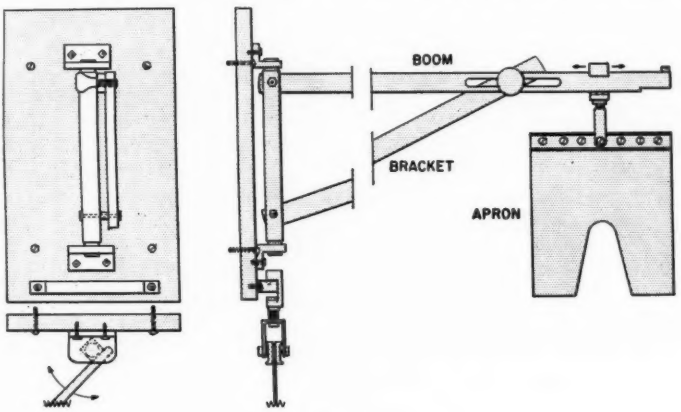

Fig. 1.

* 319 First Savings and Loan Building, Saginaw, Michigan.

square leaded-rubber apron is fashioned with a deep inverted U-shaped cutout at its lower edge so as to drape snugly over the mandible, alongside the neck, and down to the surface of the x-ray table. Several aprons are prepared for use with patients of different size. The apron is clamped between steel bars along its upper edge and is suspended from a horizontal cantilever boom by a sliding hook which permits both lateral and rotary adjustment. The boom is mounted on the wall adjacent to the x-ray table and is hinged at the wall, thus allowing excursion in the patient axis. This feature also permits swinging the boom against the wall when not in use. The lower diagonal boom-bracket is slotted into the boom with a screw-knob lock and this feature provides vertical excursion, since boom and bracket are also vertically hinged at the wall mounting. The screw-knob locks the boom firmly at the desired elevation. Screens hang on a wall rack when not in use.

A SIMPLE DEVICE FOR POSITION DETERMINATION DURING MYELOGRAPHY

I. MELBOURNE GREENBERG, M.D.*

Neurosurgical Service, Beth Israel Hospital, New York, New York

(Received for publication August 25, 1951)

The importance of a simple device for position determination during myelography became apparent when a case of spinal cord tumor with block was being demonstrated to another observer. Before the spot films made sense, each view had to be accompanied by a description indicating the degree and direction of tilt of the table. It was therefore felt that the films would be of greater value if an apparatus could be devised to automatically register on the film the direction and the degree of table angulation during the process of myelography. The simple device described below serves this purpose.

The device at first consisted of a sealed tube, half filled with pantopaque applied by adhesive tape to the under side of the fluoroscopic screen. This demonstrated the appearance of the fluid at various tilt levels in the manner of a carpenter's level. It was thus possible to indicate on the film the movement of the myelographic fluid in the same direction and in the same degree as the fluid in the tube. Subsequently a second method was utilized, consisting of a freely moving ball bearing, in a sealed pathway between two inverted protractors. The angles are indicated by lead numbers marking the divisions between zero and 90° to either side. The apparatus is made of lucite and assembled as shown in Fig. 1.

With this instrument, the interpretation of films becomes simplified. One first determines the cephalad and caudad orientation of a given myelogram, and then directly reads the declination by the location of the opaque ball. This automatically indicates, in a given view, the degree and direction of tilt of the patient. In a complete block, it is possible to demonstrate the high degree of table angulation without passage of dye. Similarly, the mobility of pantopaque after previous myelography can be recorded (Fig. 2). Furthermore, in partial block, the upper and lower limits of the lesion are more easily demonstrated.

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* Resident in Neurosurgery, Service of Dr. Leo M. Davidoff.

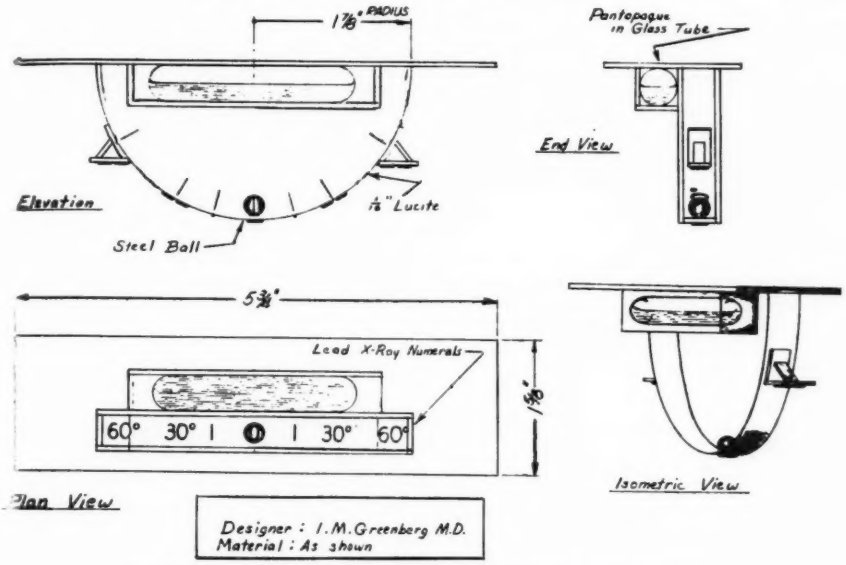

FIG. 1. Diagram of device. It is now mounted so as to slide back and forth under the fluoroscopic screen.

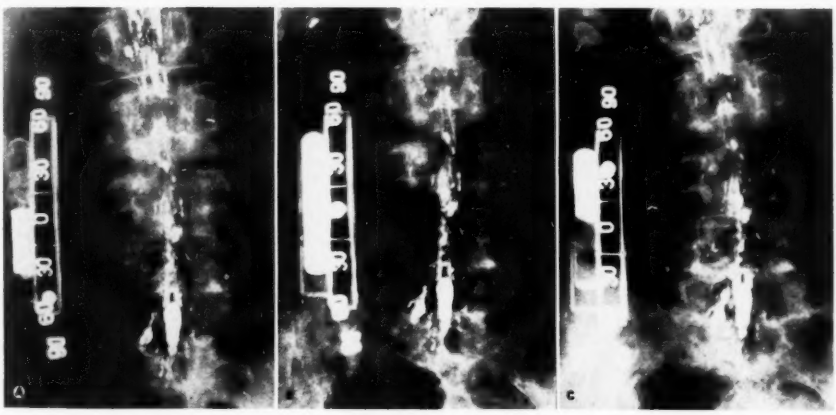

FIG. 2. Case #68060. The problem was that of dye mobility after previous myelography. (A) Patient standing at an angle of almost 60°. (B) Patient horizontal. (C) Patient tilted so that the head is down 30°. These three films provide a permanent record of dye immobility through a wide range of table tilt.

SUMMARY

A method* is presented by which the direction and the degree of table angulation during myelography is automatically recorded on the film. This is particularly important when films are viewed by someone other than the person who produced them, or even by the same person viewing them at a later date.

Other means for recording position during myelography are being investigated. Other fields are being consulted as to the aid that this type of instrument may offer.

The author is indebted to Dr. Leo M. Davidoff for his helpful suggestions.

* This device can be obtained from x-ray equipment manufacturers or Dr. I. M. Greenberg, 736 West 173rd St., New York 32, N.Y.

NOTICES

AMERICAN BOARD OF NEUROLOGICAL SURGERY

The following specialists were certified at a meeting of the American Board of Neurological Surgery in New Haven, Connecticut, October 25–27, 1951.

AMES, RICHARD H. 153 Bishop St., Greensboro, N. C.
ERB, HOWARD R. Union Bank & Trust Bldg., Bethlehem, Penna.
GAY, JAMES R. 350 East Broad St., Columbus 15, Ohio
HUNTER, CURWOOD R. 2314 Auburn Ave., Cincinnati 19, Ohio
JOHNSON, ALEXANDER C. 200 Medical Arts Bldg., Great Falls, Mont.
KAPLAN, HARRY A. 19 Grace Court, Brooklyn 2, N. Y.
KIEFER, EDWARD J. 324 East Wisconsin Ave., Milwaukee 2, Wis.
KRISTOFF, FREDERIC V. Cincinnati General Hospital, Cincinnati 29, Ohio
LISLE, A. C., JR. 1200 North Walker, Oklahoma City, Okla.
LUCE, JAMES C. U. S. Naval Hospital, Chelsea 50, Mass.
MACK, ERNEST W. 1155 Wells Ave., Reno, Nev.
MUEHLIG, WILBUR A. 636 Medical Arts Bldg., Omaha 2, Neb.
PARENTEAU, ANDRE 847 Cherrier St., Montreal, Canada
PERLMUTTER, ERWIN 716 DuPont Bldg., Miami 32, Fla.
PETERSON, CARL A. 67 East 59th St., New York, N. Y.
PFEIL, EDGAR T. Brooke General Hospital, San Antonio, Texas
REHFELDT, FREDERICK C. 1705 Medical Arts Bldg., Fort Worth 2, Texas
REYES, VICTOR A. 1115 San Andres St., Malate, Manila, R. of Philippines
SCHEUERMAN, WALTER G. 210 West State St., Trenton, N. J.
SMITH, FRANK P. Strong Memorial Hospital, Rochester 20, N. Y.
SMITH, W. EIDSON Medical Arts Bldg., Knoxville, Tenn.
STRAIN, RICHARD E. 716 DuPont Bldg., Miami 32, Fla.
WEAVER, EDGAR N. 203 Carlton Terrace Bldg., Roanoke, Va.
WEISS, EUGENE K. 724 First National Bank Bldg., Scranton 3, Penna.

AMERICAN NEUROLOGICAL ASSOCIATION

At the 76th annual meeting of the American Neurological Association held in Atlantic City, New Jersey, June 18–20, 1951, the following officers were elected for the year 1951–1952: President, Dr. S. Bernard Wortis; President-Elect, Dr. Hans H. Reese; First Vice-President, Dr. Frederick P. Moersch; Second Vice-President, Dr. A. Earl Walker; Secretary-Treasurer, Dr. H. Houston Merritt; Assistant Secretary, Dr. Charles Rupp.

FIRST INTERNATIONAL CONGRESS OF NEUROPATHOLOGY

On September 8, 1952, the First International Congress of Neuropathology will meet in Rome, Italy. The officers elected are: Honorary Presidents, Dr. U. Cerletti (Italy), Dr. J.G. Greenfield (United Kingdom), Dr. G.B. Hassin† (United States), Dr. J. Lhermitte (France), Dr. O. Vogt (Germany); President, Dr. Mario Gozzano, Rome; Secretary General, Dr. Armando Ferraro, New York.

The meeting will last for six days. In the morning sessions, assigned topics will be presented by qualified investigators from various countries. In the afternoon, discussions and individual papers dealing with the morning topics will be presented.

The following topics were chosen at the preliminary meeting of the Chairmen of the various national committees, which was held in Paris on May 30–31, 1951.

* Deceased October 28, 1951.
† Deceased August 15, 1951.

First day: Pathology of demyelinating diseases. Second day: Vascular diseases. Third day: Schizophrenia. Fourth day: Mental deficiencies. Fifth day: Senility. Sixth day: Special histopathologic and histochemical technics.

Neuropathologists, neurologists, psychiatrists, and pathologists are cordially invited. The registration fee for active membership to the Congress has been established at $15.

Additional information may be obtained from Dr. Joseph H. Globus, Chairman, United States National Committee, 960 Park Avenue, New York City.

FIFTH INTERNATIONAL NEUROLOGICAL CONGRESS

The Fifth International Neurological Congress will be held in Lisbon, Portugal, during the middle of September, 1953. The exact dates will be announced later. Special attention will be paid to the neurosurgical aspects of the symposia. In accordance with the usual custom, one day will be devoted to excursions in the vicinity of Lisbon.

A meeting in commemoration of the birth of Cajal will be held in Madrid immediately following the conclusion of the Fifth Congress. This meeting will be sponsored by the Spanish neuropsychiatrists. Plans as to the program of the meeting, those eligible to attend it, the place and dates of the meeting and other details will be elaborated by the Spanish neuropsychiatrists. An announcement as to these matters will be made at a later date.

The officers of the Fifth Congress are: Honorary Presidents, Sir Charles Sherrington, Dr. Gordon Holmes, Professor Georges Guillain, Dr. André-Thomas, Professor Th. Alajouanine, Professor A. Egas Moniz; Honorary Vice-President, Professor A. Austregesilo; President, Professor Antonio Flores; Secretary General, Professor Almeida Lima, Hospital Julio de Matos, 53 Avenida Brasil, Lisbon; Treasurer, Dr. J. Imaginario; Assistant Treasurer, Dr. V. Ramos. The local secretary and assistant secretary, the editor and assistant editors of the Proceedings of the Congress will be appointed at a later date.

The Vice-Presidents representing various constituent countries are as follows: Belgium, Prof. Van Gehuchten; Brazil, Prof. Deolindo Couto; Chile, Prof. A. Asenjo; Denmark, Prof. Knud Krabbe; France, Prof. Raymond Garcin; Great Britain, Prof. F.M.R. Walshe; Holland, Prof. W. Sillevis Smitt; Italy, Prof. L. De Lisi; Norway, Prof. Monrad-Krohn; Spain, Prof. J. Lopez Ibor; Sweden, Prof. Nils Antoni; Switzerland, Prof. F. Luthy; Turkey, Prof. Sukru Aksel; United States, Prof. Henry Alsop Riley. Other vice-presidents to represent national groups not present at the Executive Committee meeting will be appointed at later dates. A vice-presidential position has been reserved for each country that is entitled to such representation.

The national committees will be consulted in regard to the designation of vice-presidents from the national neurological groups. It was decided that Germany and Japan should be invited to participate in the Congress of 1953.

The Portuguese National Committee will be composed of Doctors Flores, Correia de Oliveira, Almeida Lima, Imaginario, Ramos, and others who may be added.

The Executive Committee, which met in Lisbon in July 1951, selected three topics for the symposia of the Congress. The subject of each symposium and the individuals entrusted with the preparation of these special topics are as follows: (1) Cerebro-Vascular Conditions (two sessions), Drs. Egas Moniz and Alajouanine

(2) The Parietal Lobe, Dr. F.M.R. Walshe. (3) Metabolic Diseases of the Nervous System, Dr. Van Bogaert.

The program for each of these symposia will be prepared by the chairman in charge, and about four invited speakers will be selected to present various aspects of the subject. Twenty minutes will be allowed to each invited speaker for his presentation.

Individual members of the Congress may discuss any one of these topics if application is made in advance in writing to the Secretary General. Five minutes will be allowed for such discussions.

Following the prepared discussions, free discussions will be permitted from the floor, with a limit of five minutes for each discussor.

Afternoon sessions will be arranged to permit the presentation of papers on miscellaneous subjects, which will be grouped in so far as possible in accordance with the subject matter of the communications. Ten minutes will be permitted for the presentation of each one of these miscellaneous subject papers. A sufficient number of sessions will be arranged to allow for the presentation of all contributions admitted to the program by the program committee. A request for a place on the program by United States members, for these ten-minute papers, must be submitted to the Secretary of the United States committee, accompanied by an abstract in quadruplicate not exceeding 200 words, before January 15, 1953. Only active members of the Congress may submit titles to be presented during the sessions for miscellaneous communications. Each active member may present one paper. Non-members will be allowed to discuss presentations only if invited by the presiding officer of the session.

The official languages in which papers may be presented are English, French, Italian, Portuguese and Spanish.

Membership in the Congress will consist of active, associate and adjunct members. Applicants for active membership must belong to some national or local neurologic, psychiatric, neuropsychiatric or neurosurgical association or society. The fee for active membership will be $15.00.

Physicians in other specialties and individuals engaged in fields of scientific activity associated with neurology, psychiatry or neurological surgery may apply for associate membership. The fee for associate membership will be $10.00.

Members of the families of members, and non-medical individuals interested in the Congress, may apply for adjunct membership. The fee for adjunct membership will be $5.00.

Application blanks for United States nationals for all types of membership in the Congress may be obtained by writing to the secretary of the committee for the United States, Dr. H. Houston Merritt, Neurological Institute, 700 West 168th Street, New York 32, N.Y.

Each application for active membership must present endorsement by some national or recognized local neuropsychiatric or neurosurgical organization or by a neurologist or psychiatrist known to members of the United States committee.

Canadian neurologists and psychiatrists and other Canadians interested in attending the Congress should communicate with Dr. J. Allan Walters, secretary of the Canadian Committee, Medical Arts Building, Toronto.

The American Express Company has been chosen as the official travel agency for the Fifth International Neurological Congress. In order to obtain the most

satisfactory results, arrangements for travel or for hotel accommodations should be made through the American Express Company. Arrangements may, of course, be made through any travel agency, but in order to ensure the most satisfactory results it is advised that the recognized travel agency be employed for these purposes. Early application for room reservations should be made.

An effort will be made to reserve a sufficient number of various types of staterooms on some eastbound steamship sailing at the end of August or the early part of September. Similar arrangements will be made for the westbound passage toward the end of September. In all probability special tours through various parts of Portugal and adjacent countries will be arranged by the American Express Company for those wishing to take advantage of such facilities.

The support of the Congress will be provided by the membership fees and an appropriation from the national neurological association of each of the constituent countries, representing the equivalent of $1.00 for each member of the national organization.

The proceedings of the Congress will be published. They will consist of abstracts of presentations and discussions together with other pertinent details concerned with the conduct of the Congress.

As no title or abstract will be accepted by the U.S.A. committee unless at the time of submission the author is an active member of the Congress, an application blank for membership properly filled out, together with check in payment of the membership fee, should precede or accompany the title and abstract and should be addressed to Dr. H. Houston Merritt, Neurological Institute, New York 32, N.Y.

Committee for the United States Fifth International Neurological Congress: Henry Alsop Riley, Chairman; H. Houston Merritt, Secretary; John F. Fulton, Foster Kennedy,* S. Bernard Wortis, Walter Freeman, Francis C. Grant.

HARVEY CUSHING SOCIETY

Members of the Harvey Cushing Society who have papers they wish to submit for the meeting in Victoria, B.C., June 5–7, 1952, are requested to send the title and a short description of the material to the chairman of the Program Committee, Dr. William T. Peyton, University of Minnesota, The Medical School, Minneapolis 14, not later than March 1, 1952.

NEUROSURGICAL SOCIETY OF AMERICA

At the 4th annual meeting of the Neurosurgical Society of America, held at Sun Valley September 12–14, 1951, the following officers were elected: President, Dr. Joseph F. Dorsey, Boston; Vice-President, Dr. Lyle A. French, Minneapolis; Treasurer, Dr. I. Joshua Speigel, Chicago; Secretary, Dr. C.D. Hawkes, Memphis.

The membership of the society at the present time is 50.

* Deceased January 7, 1952.

ALFRED WASHINGTON ADSON

ALFRED WASHINGTON ADSON—PIONEER NEUROSURGEON
1887–1951

WINCHELL McK. CRAIG, M.D.*
Rochester, Minnesota

(Received for publication December 31, 1951)

ALFRED WASHINGTON ADSON, after a full life devoted to medicine and surgery, was approaching retirement. He had begun his medical career in the field of general surgery but fate directed his interest toward the specialty of neurosurgery. Hearing of his imminent retirement, the former fellows in neurosurgery at the Mayo Foundation, Graduate School, University of Minnesota, wished to show their devotion to and admiration for him and, on September 28 and 29, 1951, they gathered in Rochester, Minnesota, to honor him at a dinner and to present him with a token of their esteem. Most fortunate was this celebration for, without warning, less than two months later, on November 12, Dr. Adson's life came to an end in an attack of coronary occlusion.

The position of Alfred Washington Adson in the specialty of neurosurgery and the place of neurosurgery in the world and in America have been felicitously described by Earl Walker: "Although neurological surgery may have been conceived in England and spent its infancy in Europe, there is no doubt that it passed a stirring adolescence and came of age in the United States of America. To Harvey Cushing belongs much of the credit for the guidance of the growing specialty through its formative years. The growth of neurological surgery was not confined to the New England States of America—Frazier, Dandy, Sachs, Adson, Naffziger and others in widely separated parts of the country were aiding in the maturation of the specialty."

At the testimonial dinner given for him by the former fellows in neurosurgery, Dr. Adson was asked to relate some of his early experiences in the development of neurosurgery at the Mayo Clinic. His informal story was of historical value as it revealed the trend of the development of most of the surgical specialties and his relation to his own specialty. Also, it gave evidence of his forceful character, his determination to excel in neurological diagnosis and neurosurgical technic and his desire to impart to younger men those facts gleaned from his own experience that would make them better doctors.

The succeeding several paragraphs so closely follow the account that he gave that they have been treated as a quotation.

* Mayo Clinic, Rochester, Minnesota.

On July 1, 1914, having just been graduated in medicine from the University of Pennsylvania, I was admitted to the Mayo Foundation for a three-year course in general surgery. At that time I had no interest in neurosurgery nor did I ever suspect that I should devote my full time to neurosurgery.

I served as assistant to Drs. W. J. Mayo, C. H. Mayo, E. Starr Judd, Walter Sistrunk and Emil Beckman. While I was serving as first assistant to Dr. Beckman, he became ill with an infection which extended from a nasal furuncle and resulted in his death on November 7, 1916. Dr. Beckman was an exacting surgeon. His teaching created in me a desire to perfect myself and to become competent in general surgery.

Following Dr. Beckman's death, I was invited to join the staff of the Mayo Clinic as junior general surgeon and, on January 1, 1917, to become a staff surgeon. In my interview with Dr. W. J. Mayo regarding my staff duties, he said, "You will, of course, be expected to look after the few neurosurgical cases that will come to the Clinic."

I carried on in general surgery, assuming more and more of the responsibility in major cases, with the advice and assistance of the senior surgeons. In my first year of independent surgery, from November 10, 1916, to November 1, 1917, I had occasion to operate on five neurosurgical patients. I had learned that all cases of tumor of the brain and spinal cord are not hopeless. I had become impressed by the fact that patients suffering from lesions of the central nervous system are just as anxious to be relieved as are those who complain of abdominal symptoms.

The first of the five patients was a male who presented symptoms of a tumor in the right motor cortex. Dr. Walter Shelden of the neurological department was convinced of the diagnosis and of the location of the lesion and he prevailed on me to perform craniotomy. On December 7, 1916, I turned down an osteoplastic flap over the right parietal area. There was the tumor situated under the dura and attached to it. After controlling the bleeding by the cumbersome methods of that day, I proceeded to incise the dura about the tumor, protecting the brain with cotton. The tumor, then, was easily removed. The patient made a satisfactory recovery and returned to work. I heard from him annually at Christmas time until 1938.

The second case was not so dramatic, and it taught me that if I were to attempt more neurosurgery it would be necessary for me to study neuro-anatomy, make dissections and, probably, improve on the instruments and methods employed for hemostasis.

The case was one of trigeminal neuralgia in which the peripheral mandibular branch had been avulsed and, later, alcohol had been injected without relief. On February 16, 1917, I proceeded with transtemporal section of the sensory root. What a nightmare! I used a headlight, Cushing retractors and, to control hemorrhage, gauze strips. Blood from the middle meningeal artery squirted all over the place. I tried to occlude the foramen spinosum with a wooden plug but I was unable to find the foramen in the pool of blood. After several hours of mental agony for me, I filled the middle fossa with gauze strips and gave the patient 750 cc. of physiologic saline solution to alleviate the symptoms of surgical shock. Four days later, I removed the packs with fear of another hemorrhage. Fortunately, the meningeal artery had thrombosed; the sensory root was brought into view and I avulsed it. However, I regret to say that the avulsion was not complete. Thus, it became necessary to operate again two months later. The patient's pain was relieved, but unfor-

tunately, he was left with partial palsy in the distribution of the sixth nerve and temporary unilateral facial palsy.

The third case was that of a girl who presented symptoms of increased intracranial pressure with signs suggestive of a lesion of the left frontal lobe, presumably a tumor. An osteoplastic flap was elevated on June 6, 1917, but instead of uncovering a tumor, an abscess of the left frontal lobe was encountered. This I drained, and the girl recovered after much difficulty with osteomyelitis of the bone flap. Now it became more obvious than ever that if I were to continue to deal with neurosurgical problems, I would have to study neurology and attempt to integrate allied services such as neurology, ophthalmology, pathology, radiology along with my efforts in surgery, much as the Mayo Clinic was doing with problems of general medicine and surgery.

The patient of the fourth case was a woman who presented the symptoms and findings of a pituitary tumor. Loss of the temporal visual fields and roentgenograms revealing an enlarged sella suggested a chiasmal lesion. By this time, I wished to make a transfrontal approach to the pituitary gland, having designed an illuminated brain retractor and special forceps for removing adenomas of the gland. The operation was performed on August 22, 1917, and subsequently the patient's vision returned to normal.

In the fifth case the patient was a man who came to the Clinic suffering from spastic paraplegia. Dr. Shelden localized a lesion, presumably an intraspinal tumor of the thoracic cord. On October 30, 1917, I proceeded with the operation after completing a list of general surgical cases. However, I had not anticipated a gallery of such distinguished guests as I was about to have. Sir Berkeley Moynihan, later Lord Moynihan of Leeds, and then on active service as a high officer in the British Army; Dr. Duval, surgeon of the French Army; and Professor Bastianelli of the Italian Army were visiting the Clinic that morning in their tour of the United States, soliciting physicians as volunteers for their respective services. Moynihan was the first to enter the operating room and inquire as to the nature of the operation that was about to be performed. When he learned that a cord tumor was suspected, he decided to stay and see the procedure through, instead of joining Drs. Will and Charlie at lunch. Dr. Duval, Professor Bastianelli and others then entered the room. Drs. Will and Charlie did their best to relieve my emotional stress by urging the guests to join them for lunch. The army surgeons insisted on staying. Fortunately, removal of the first lamina revealed an intradural mass. It proved to be a meningioma. The patient's recovery was uneventful, and when he returned home, it was no longer necessary for him to use his crutches.

It was the observation at this surgical clinic, "the removal of an intraspinal tumor," so it is reported, that prompted Moynihan to say that he had seen a high school boy doing neurosurgery at the Mayo Clinic. The fact that such distinguished men thought it worth while to remain to see an intraspinal tumor removed made a profound impression on me.

Along with the growth of neurology, a similar increase took place in neurosurgery, and it was difficult for me to decide whether to remain a general surgeon or to devote all my time to neurosurgery.

It was not until October 28, 1921, while I was attending an annual meeting of the American College of Surgeons, in Philadelphia, that I reached the final decision. I was there to be made a fellow and to take part in a neurosurgical program. Cushing presented a paper on brain tumors. Frazier discussed trigeminal neuralgia. Elsberg

spoke on spinal cord tumors and I reported my study of nerve regeneration and reviewed cases encountered at the Clinic. Following the evening program, Dr. Will came to my room in the Hotel Bellevue-Stratford and stated that he was convinced that there was a future in neurosurgery. He advised me to give up general surgery and to devote all my time to the specialty. This I agreed to do providing I would be allowed to create a department so integrated with the rest of the Mayo Clinic that we would be one of its sections.

From that date the neurosurgical department began to develop. It grew only because of the addition of competent staff men and the support of men in associated fields.

ANCESTRY, EARLY DAYS, SCHOOLING, ACADEMIC AND CIVIC RECOGNITION

In the early days of the nineteenth century, a Norwegian sailor named Martin Adson came to this country from Stavanger, Norway. He followed the trend of the time, journeyed west and settled in Iowa. He married Anna Bergeson and began farming near Terril, Iowa. To this couple was born Alfred Washington Adson on March 13, 1887. Alfred attended the public schools of Terril and was graduated with honors from high school in 1908.

Ambitious and with a keen mind which was recognized by his teachers, he then entered the University of Nebraska where he embarked on a scientific course in preparation for the study of medicine. In his junior year at the University of Nebraska, he met and married Lora Grace Smith, daughter of Alfred Truman Smith of Republican City, Nebraska.

Graduating from Nebraska with the degree of bachelor of science in 1912, he transferred to the University of Pennsylvania and received the degree of doctor of medicine in 1914. Following his graduation he received an appointment as fellow in general surgery in what became the Mayo Foundation, Graduate School, University of Minnesota. In the meantime he had received the degree of master of arts from the University of Nebraska in 1918. The honorary degree of doctor of science was conferred later by the University of Nebraska and by St. Olaf College, both in 1948.

Dr. Adson received the degree of master of science in surgery from the Mayo Foundation, Graduate School, University of Minnesota, in 1918. He advanced to the position of professor of neurosurgery in the Mayo Foundation, heading the Section of Neurosurgery in the Mayo Clinic from January, 1921, to October 1, 1946, when he became senior neurosurgeon.

At the time of the centennial of the state of Minnesota in 1949, Dr. Adson was selected as one of Minnesota's "One Hundred Living Distinguished Citizens."

MINNESOTA STATE MEDICAL ASSOCIATION AND AMERICAN MEDICAL ASSOCIATION

Not only was Alfred Washington Adson interested in medicine and surgery in his own community, but throughout most of his professional life

he was active in the councils of the Minnesota State Medical Association and the American Medical Association. He became president of the Minnesota State Medical Association in 1937, and at different times he served on state committees having to do with university relations, social workers, medical economics, Minnesota Medical Service, insurance, public policy and the work of statewide congressional committees. In 1943, he was appointed as one of the original members of the Council on Medical Service and Public Relations of the American Medical Association, in which capacity he served until 1951.

MINNESOTA STATE BOARD OF MEDICAL EXAMINERS

Because of his interest in advancing the ideals and standards of medicine, Dr. Adson was appointed to the Minnesota State Board of Medical Examiners in 1929 by Governor Christianson, and because of his capability and unbounded interest and enthusiasm, he was reappointed by Governor Olson, Governor Thye and Governor Youngdahl. He served from 1929 until 1951 in the capacity of president and member of the board, and throughout the years exerted an influence that was invaluable in the promotion of better medicine for the entire country and especially for the state of Minnesota.

NEUROSURGERY

The greatest impact of this industrious, enthusiastic, irrepressible, ingenious individual was felt in the specialty of neurosurgery.

Entering the field as a pioneer he brought to the specialty new ideas and practical applications of neuro-anatomy, neurophysiology and neuropathology, as is attested in his bibliography. He early manifested an interest in tumors of the brain, tumors of the spinal cord and peripheral nerve surgery and he spearheaded surgery of the sympathetic nervous system.

Interested in the teaching of his surgical specialty, he was a founder member of the American Board of Surgery and of the American Board of Psychiatry and Neurology. Realizing that neither of these boards served the purpose of furthering the specialty of neurosurgery, he, along with others, sponsored the formation of the American Board of Neurological Surgery and served in the capacity of a member of this board from its inception, ending his career as chairman.

SURGERY OF THE SYMPATHETIC NERVOUS SYSTEM

Soon after Royal and Hunter postulated relief of spastic paralysis by ramisection of the sympathetic nervous system, Adson advanced the hypothesis that any improvement that might have been apparent was attributable to the effect on the sympathetic nerve supply to the blood vessels and, consequently, on increased circulation to the part. He and George Brown investigated this hypothesis in treatment of Raynaud's disease, scleroderma and thromboangiitis obliterans. Clinical improvement resulted and this treatment was applied for chronic arthritis and for progres-

sive, uncontrollable hypertension. While the clinical results in arthritis were temporary, the effects on vascular diseases such as Raynaud's disease, thromboangiitis obliterans and arteriosclerosis were so effective that use of sympathectomy in treatment of these diseases has become universal.

Adson's interest in the effect of surgery of the sympathetic nervous system in treatment of hypertension really began when he and Rowntree decided to carry out lumbar and cervicothoracic sympathetic ganglionectomy. The results of these operations were disappointing. He then conceived the idea of dividing the anterior roots of the spinal cord in the thoracic and lumbar regions intraspinally since they carried sympathetic fibers. Following this procedure, the effect on blood pressure was phenomenal, but the disability and hazards of the operation were too great. About this time operations on the splanchnic nerves were being carried out and subdiaphragmatic resection of these nerves was combined with lumbar sympathetic ganglionectomy to form one of the standard operations for relief of hypertension. At the time of his death, Adson was following a group of patients who had undergone ablation of the entire celiac ganglion. He thought that the resulting denervation of the splanchnic region might result in a maximal fall of blood pressure. Also, he contended that the adrenal glands should be examined at the time of operation and resection undertaken in selected cases.

TRIGEMINAL NEURALGIA

The painful syndrome of trigeminal neuralgia challenged the diagnostic acumen and the therapeutic ingenuity of physicians for many years. Adson aptly described the therapeutic approach in the report of his second case, quoted earlier in this account. He accepted the challenge and his contributions to the technic of the operation for relief of this painful syndrome comprise the vertical incision, the sitting posture, the ligation of the middle meningeal artery and the preservation of the motor root. One of his neurosurgical colleagues, in a recent book review, commented as follows: "Anyone who has assisted at an operation for cutting the sensory root of the fifth cranial nerve for the relief of trigeminal neuralgia with the patient lying down can appreciate the contribution that Adson made to the surgery of that disease and the refinements he brought to the surgical procedure."

CERVICAL RIBS AND THE SCALENUS ANTICUS SYNDROME

Compression of the brachial plexus by anomalous cervical ribs and scalene muscles early interested Adson. He thought this was a neurosurgical problem which previously always had been approached from an orthopedic standpoint. Unfortunately, the clinical syndrome frequently was not relieved and sometimes was worsened after the ribs had been attacked from a posterior approach. Adson postulated that if the brachial plexus was being compressed, an anterior approach, whereby the plexus could be seen, was more practicable. The first operation of this sort that he attempted was going smoothly, and he had resected the anterior scalene muscle, when the patient's condition was such that the operation had to be discontinued. Much to Adson's

delight and surprise, the following day the patient's symptoms had disappeared; and thus developed his scalenectomy for relief of the syndrome. Later he modified his ideas about the simple procedure of scalenectomy and removed the cervical rib if the pressure on the brachial plexus was not relieved by the more simple procedure. The result of this type of operation has influenced the thinking on neurosurgical procedures for relief of compression of the brachial plexus by cervical ribs or scalene muscles.

CEREBROSPINAL RHINORRHEA

The escape of cerebrospinal fluid from the subarachnoid space always has been fraught with danger of infection. This is especially true of the intranasal dripping associated with leakage through the cribriform plate. Intranasal meningoceles, and postoperative and post-traumatic fistulas have challenged the ingenuity of the surgeon for many years. After many attempts at repairing these fistulas, Adson finally arrived at the conclusion that the intracranial approach was the solution. Exposing the cribriform plate as well as the overlying dura by transfrontal craniotomy, the tear in the dura was repaired, the opening in the floor of the skull was closed with bone wax and tantalum plates, and thus escape of cerebrospinal fluid was controlled and the danger of retrograde infection was averted.

INSTRUMENTS

Most of the pioneer surgeons who attempted operations on the central nervous system realized the need of instruments to facilitate exposure, control of hemorrhage and delicate resection of nerves and portions of the brain and spinal cord. Adson devised ingenious instruments, some of which were improvements of similar instruments, but various clamps, scalpels, retractors and scalp clips bear his name, attesting to his various interests in carrying out more nearly perfect operative procedures.

HONORS

Honors come to him who attains a pinnacle in his chosen profession. So it was with Adson, and some of these honors have been mentioned in a previous paragraph. No attempt will be made here to include lists printed in biographical reference works. In general, however, American surgical societies gave Dr. Adson honorary membership, and many foreign societies numbered him among their illustrious members. Editorial boards and editorial staffs turned to him as consultant for their periodicals, and he was always generous with his time and thought in such work.

Of all the honors that came to him, however, he appreciated and valued most the final honor conferred on him by the former fellows in neurosurgery just two months before his untimely death. The convening of these younger men brought to him forcibly how much he meant to the entire specialty of neurosurgery and especially to them. Almost prophetic was his address at the dinner in his honor when, in serious vein, he said, "I would rather you came to honor me now than to attend my funeral."

FAMILIAL HAEMANGIOMATA OF THE CEREBELLUM

REPORT OF THREE CASES IN A FAMILY OF FOUR

HENRIK O. TONNING, M.D.,* RUPERT F. WARREN, M.D.,† AND HOWARD J. BARRIE, B.M.‡

Department of Neurosurgery, Christie St. Hospital (D.V.A.), Toronto, and Department of Pathology and Division of Neuropathology, University of Toronto, Ontario

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HAEMANGIOBLASTOMATA of the central nervous system are isolated lesions unless they constitute part of the hereditary disease known as Lindau's Syndrome, when they may be associated with angiomata of the retina and spinal cord, multiple cysts of the kidneys and pancreas and even renal carcinoma.

Of 22 haemangioblastomata met with in the Toronto General Hospital between 1932 and 1947, 3, all in members of one family, were examples of Lindau's Syndrome. This underlines the importance of taking a careful family history when vascular tumours are discovered in the brain. This is a record of the family involved and of the findings in 2 of its members who came to necropsy. It illustrates nearly all the known features of Lindau's Syndrome. The ophthalmological findings in this family have been described in detail by Dr. A. E. MacDonald.[2]

The family consisted of 4 children (Fig. 1), of whom 2 have died of the disease, 1 is known to have it but is alive and well, and 1 is apparently well apart from a haemangioma of the eyelid. The mother almost certainly died of the disease, for her eye was removed at the age of 22 and she later died from a tumour in the brain.

Case 1. Miss E.R., aged 23, was admitted on Feb. 4, 1936, with a history of headaches and nausea for 6 months and vomiting for 1 month. A year and a half before admission, while standing, she suddenly and painlessly became blind in the left eye from an intra-ocular haemorrhage.

Examination. There was papilloedema of the right eye. The remainder of the neurological findings were negative.

1st Operation. Cerebellar exploration by Dr. K.G. McKenzie disclosed a very vascular tumour in the lower half of the left cerebellar hemisphere causing direct pressure on the medulla. It was the size of a large walnut. A large venous channel, $\frac{1}{8}$" in diameter, ran from the tumour and into the transverse sinus. Several large thin-walled veins communicated with this main vessel. Puncture of the left cerebellar hemisphere showed that the tumour was firm, solid, and unusually vascular. Decompression only was attempted.

Course. Following operation she received an intensive course of x-ray therapy and was discharged after 65 days.

* Department of Neurosurgery, Christie St. Hospital (D.V.A.), Toronto.
† Department of Pathology and Division of Neuropathology, University of Toronto.
‡ Department of Pathology, University of Toronto.

In May 1936, she was re-admitted for investigation because of vomiting, loss of appetite, drowsiness and crying spells. The symptoms were considered due to post-radiation reaction and she returned to her home after 14 days.

2nd Operation. In May 1937, Dr. A. E. MacDonald removed her painful blind eye and found a haemangio-endothelioma in it which had caused the sudden haemorrhage 2 years previously.

Course. Two years later there was papilloedema in the right eye and inco-ordination as shown by the finger-to-nose test on the left side.

3rd Operation. A re-exploration in August 1939 showed a large, well-demarcated,

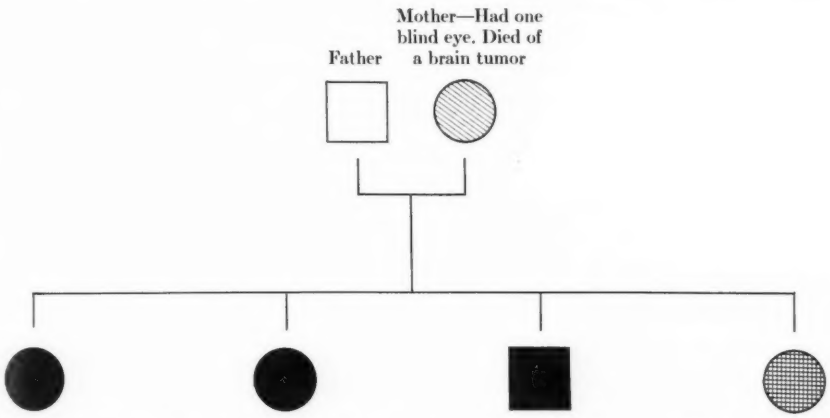
Mother—Had one blind eye. Died of a brain tumor
Father
E.R. (Case 1). Died of von Hippel-Lindau's disease with polycystic disease (1947)
L.S. (Case 2). von Hippel-Lindau's disease. Died of renal carcinoma (1948)
W.R. (Case 3). von Hippel-Lindau's disease. Alive and well (1951)
Miss R. (sister of Cases 1, 2, and 3). Haemangioma of eyelid.

FIG. 1. Shows the distribution of the disease in this family.

solid tumour to be nearly replacing the left cerebellar hemisphere. The tumour was removed and patient made an uneventful recovery.

Pathological Examination. The tumour was surrounded by a poorly-defined fibrous capsule and many thin-walled blood vessels. Microscopically it was a haemangio-endothelioma composed of masses of swollen vacuolated endothelial cells surrounded by very thin-walled vessels (Fig. 2). No mitotic figures were seen.

Course. In 1947 her headaches and papilloedema returned.

4th Operation. In another exploration of the cerebellum two large tumours were found. One was the size of a hen's egg and occupied the place of the left cerebellar hemisphere. It had infiltrated downwards into the neck muscles. A smaller tumour connected to the first was found in the roof of the 4th ventricle. Both of these were removed and it was then apparent that the medulla had been severely compressed.

Course. The patient died 3 days after operation.

Pathological Examination. The recurrent tumour tissue resembled the first biopsy.

Necropsy. Gross findings: (Recurrent haemangio-endothelioma of left cerebellar

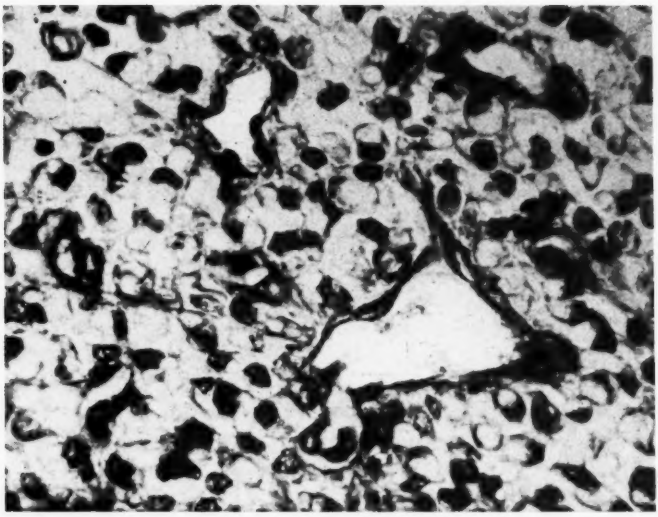

FIG. 2. *Case 1.* Photomicrograph (×660) of haemangioblastoma removed from left cerebellar hemisphere.

FIG. 3. *Case 1.* The left kidney and pancreas, showing multiple cysts in both organs

hemisphere); recent haemorrhage into medulla; miliary meningiomata of sella turcica; multiple cysts of pancreas, kidneys and lungs; regional interacinous fibrosis of pancreas; cortical infarct of left kidney; bilateral bronchopneumonia; fibrous pleural adhesions; fibromyoma of uterus.

It was not possible to recognize any remaining tumour tissue in the necrotic material lining the operative cavity. The medulla was compressed and contained several haemorrhages. Multiple petechial haemorrhages were also present along the whole extent of the corpus callosum and into the septum pellucidum.

The pancreas weighed 200 gm. and measured 22 cm. in length, 7 cm. in width

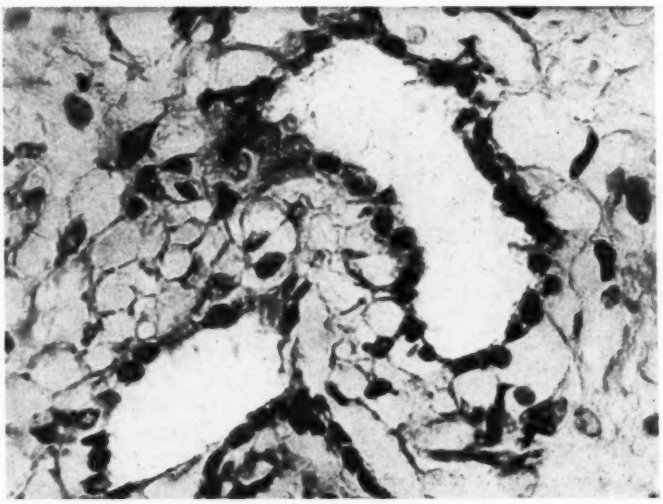

FIG. 4. *Case 1.* Photomicrograph of pancreas (×660). The two small pancreatic cysts are lined by low cuboidal epithelium.

and 6 cm. in thickness. It was made up almost entirely of grey and light brown cysts of varying size, measuring from 0.1 to 2 cm. in diameter (Fig. 3). The larger cysts lay just to the right of the groove for the inferior mesenteric vessels. The cysts contained clear fluid. Small cysts were often clustered. The cyst walls were thin, grey, translucent and encircled by a narrow zone of fibrous tissue containing an occasional tiny island of pancreatic tissue.

The left kidney weighed 110 gm. and the right 105 gm. The kidneys were alike. On their surfaces were many cysts of varying size, measuring from 0.5 to 2 cm. in diameter (Fig. 3). The left contained 30, and the right 20 of these cysts. Some were flat, others were raised above the surface of the kidney, and contained yellow or brown, clear fluid. The capsule stripped easily over these cysts which were thin-walled and confined to the surface of the cortex. A small cortical infarct was present in the upper pole of the left kidney. The remainder of the kidney parenchyma was normal.

There were moderately dense, fibrous adhesions over the whole of the left lung. On the peripheral surface of the upper lobe of the right lung, 8 cm. from the apex,

was a small, soft, slightly elevated, dark bleb surrounded by normal lung tissue. It measured 4 mm. in diameter. Patchy bronchopneumonia was present in the right middle, and the lower lobes of both lungs.

In the anterior wall of the uterus was a fairly large, encapsulated fibromyoma. In the upper pole of the right lobe of the thyroid was a small, simple nodular adenoma.

Microscopic Findings. The pancreatic cysts were usually situated at the periphery of lobules in which the acini were atrophied and separated or replaced by loose

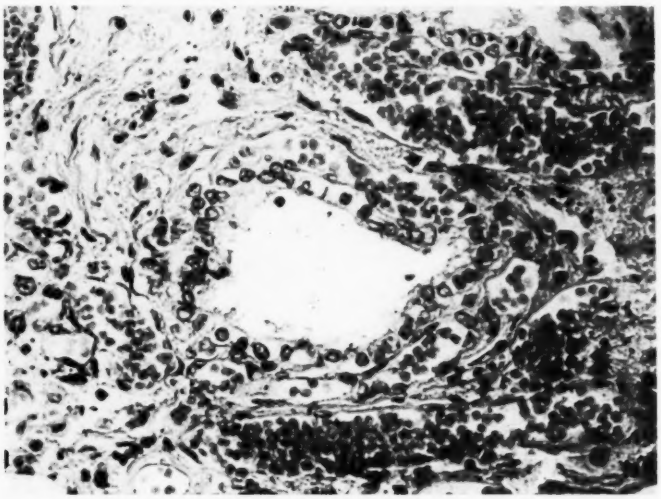

FIG. 5. *Case 1.* Photomicrograph (×300) of upper lobe of right lung. The same cyst is lined by cuboidal epithelium and surrounded by wide congested sinusoids.

strands of connective tissue containing scanty aggregates of lymphocytes. The cysts were in varying stages of development, the smaller closely resembling ducts. They were lined by low cuboidal cells (Fig. 4), and surrounded by fairly wide bands of loose connective tissue. In a small number, the lining resembled endothelium, and small papillae, composed of a fine fibrous core lined by epithelium, projected into their lumina.

Lobules of normal acini were few. In these the ducts were lined by normal columnar epithelium and surrounded by loose strands of connective tissue. The islet cells were well preserved.

The renal cysts were lined by low cuboidal epithelium. They were surrounded by fairly dense hyaline collagen in which were a few hyalinized glomeruli and blood vessels and they resembled the common retention cysts of the kidney.

The small bleb seen under the pleura in the upper lobe of the right lung was caused by a collection of varying-sized cysts lined by low cuboidal epithelium with pale, oval nuclei. These did not contain blood but in the surrounding loose connective tissue were many enlarged congested sinusoids (Fig. 5). Deeper in the lung tissue and immediately adjacent to a pulmonary vein was a collection of similar spaces. These cysts were in very close relation to many enlarged sinusoids filled

with red blood cells. The sinusoids often indented the walls of the cysts and were sometimes seen in the connective tissue of the septa in the absence of cysts (Fig. 6).

In random sections from each of the lower lobes of both lungs were many collections of similar cysts. Some were fairly large, and contained homogeneous pink-staining material and were lined by flattened cuboidal epithelium.

The cysts were mainly found in the sub-pleural region, or immediately adjacent to small bronchi and blood vessels. In some areas, collections of small cysts distorted the bronchi and separated them from the adjacent blood vessels.

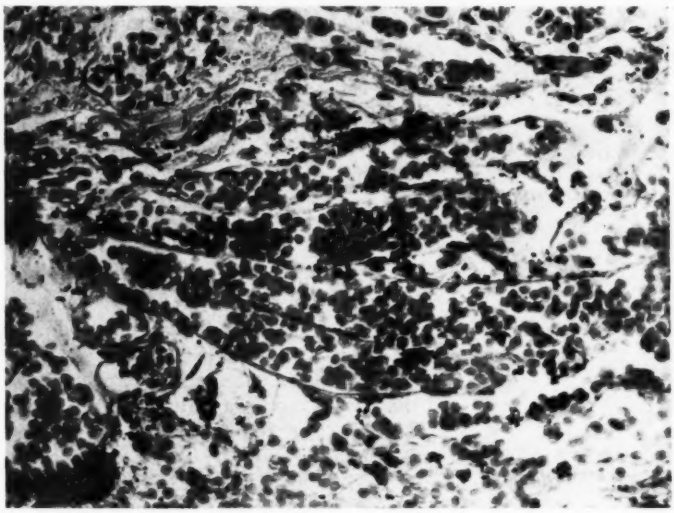

FIG. 6. *Case 1.* Photomicrograph (×300) of lower lobe of right lung, showing congested sinusoids in the absence of cysts.

There was no apparent communication between the cysts and the bronchi or alveoli. There was no elastic tissue or smooth muscle in their walls.

In the brain there was no evidence of tumour tissue. Outside the capsule of the pituitary gland were several microscopic meningiomata.

Case 2. Mrs. L.S., aged 29, sister of Case 1, was admitted on April 29, 1938. She complained of loss of central vision in the right eye for 1 year, severe frontal headaches for 6 months, repeated attacks of nausea and vomiting, and at times a feeling of falling. Since infancy she had had a bilateral equinus deformity of the feet.

Examination. There was a lower nasal defect in her visual field and she had bilateral papilloedema. The remainder of the cranial nerves were normal. In walking and standing with the eyes closed, she was found to stagger to the right. There was slight inco-ordination on the right side.

A ventriculogram showed well-developed dilatation of the lateral ventricles with an enlarged well-filled 3rd ventricle.

1st Operation. On exploration of the posterior cranial fossa, a large firm tumour was seen in the upper part of the left cerebellar hemisphere. It was attached to the

dura, the lateral sinus and the tentorium by large thin-walled vessels, which were filled with bright red blood. The tumour was very vascular. The entire neoplasm was removed with difficulty and was about the size of a large walnut. On section it was found to contain a large cyst with a nodule of tumour in its wall.

Microscopic Examination. The tumour was identical with those taken from Case 1.

Course. The patient did well for 1 year, at the end of which time Dr. A. E. MacDonald diagnosed a haemangioma of the right eye which he treated by the application of radon seeds. Examination showed marked inco-ordination of the left arm and in both legs and staggering to both sides with the eyes closed. Sensation was poor in all divisions of the left 5th cranial nerve and hearing was diminished in the left ear. It was apparent there was a recurrence of the cerebellar tumour.

2nd Operation. The left cerebellar hemisphere was re-explored. About 1 cm. deep in the middle of the left cerebellar hemisphere a cystic cavity was found filled with yellow fluid. Around this several large vessels were observed. They were ligated and the cavity was drained.

Microscopic Examination. Section of a biopsy showed a very cellular haemangio-endothelioma with cystic degenerative changes, similar in general pattern to the original tumour.

Course. Postoperatively she continued to complain of some unsteadiness and of deafness in the left ear, but showed no evidence of further recurrence. She died in November 1948, 6 years after the removal of her second cerebellar tumour.

Necropsy was done elsewhere. There was no evidence of recurrence of tumour in her atrophied left cerebellar hemisphere but a carcinoma was almost completely replacing one of her kidneys, and there were multiple nodular metastases in one of her lungs.

The renal tumour was forwarded to us. Microscopically it was composed in part of big cells with homogeneous pink cytoplasm and in part of cells whose cytoplasm was almost entirely replaced by vacuoles. There was occasional tubular structure and the tumour was divided into bands by coarse collagenous septa. It had all the features of a classical clear-cell carcinoma of the kidney.

Case 3. W.J.R., an Air Force Pilot aged 28, was brother of Cases 1 and 2. He was admitted in January 1943, complaining of headaches increasing in severity for 8 months, nausea and vomiting, periodic attacks of double vision, occasional blurring of vision in the right eye, clumsiness in the right leg, and loss of recognition of position of right foot.

Examination. There was early papilloedema, more marked on the right than on the left. The sensation in the palate and the gag reflexes were diminished. There was diminished sensation to light touch and pin prick in the right arm. Position sense in the right foot was impaired. There was no inco-ordination of the limbs. On walking with eyes closed the patient tended to deviate and fall to the right. The patient had a mild hypertension with considerable variation in different positions: Lying 150/90; sitting 150/110; standing 150/120.

A ventriculogram showed moderate dilatation of the ventricles suggesting a posterior fossa lesion.

Operation. On exploration of the cerebellum, a solid encapsulated tumour, the size of a large walnut, was found in the right cerebellar hemisphere and was removed. Numerous large blood vessels were seen on the surface of the tumour. The speci

men measured 3.5×3×1.5 cm., and weighed 9 gm. It was greyish-brown, with an irregular surface, and had many small blood vessels coursing over it.

Microscopic Diagnosis. Haemangio-endothelioma, indistinguishable from the tumours in Cases 1 and 2.

Course. In February 1947 there was no evidence of recurrence of the cerebellar lesion and the patient was in excellent health, but ophthalmoscopic examination showed a small left-sided retinal haemangioma which had not been present previously. This tumour was treated by Dr. A. E. MacDonald with radium applications. When last seen in September 1951, the patient was in good health.

DISCUSSION

The main interest of Lindau's Syndrome to us is that although, as Lindau[1] pointed out, many of the lesions seem clearly attributable to a developmental defect, there must also be a persistent alteration of tissue reactivity because new lesions may develop throughout life. In this it differs from the developmental abnormalities caused by such a damage to the foetus as is produced by the virus of German measles. The latter may cause developmental abnormalities in the heart but any further lesions that occur are but secondary to the altered dynamics of the circulation.

Lindau[1] attributed the initial trouble in his syndrome to a failure in the integration between mesodermal and epithelial components. In the case of the pancreatic cysts, which he considered one of the most characteristic lesions of the syndrome, this would lead to the separation of small clusters of epithelial cells which later become cystic. Figs. 5 and 6 show beautifully how such a lesion in the lung can have dual features from such a lack of integration. There is one epithelial-lined cyst and an adjacent cluster of thin-walled blood vessels. The latter are evenly supported and neither here nor in the cysts of the pancreas can one properly call the lesion progressive. The epithelial cyst might become larger from accumulation of more fluid and the blood vessels might become telangiectatic from altered dynamics but these would be secondary changes and in these particular lesions we are dealing with a relatively stable error of development which probably occurred in utero.

One could also imagine a cerebellar vascular abnormality becoming telangiectatic and causing symptoms, but a glance at Fig. 2, which is representative of the tumours in all 3 of our cases, shows that these were progressive cellular tumours and not just telangiectases. This lesion must thus be considered in a different category from those arising in utero. The development of a renal carcinoma in Case 2 is even more challenging and this is not an isolated occurrence for Lindau reported that in 6 out of his original 15 cases there were similar tumours.

We may accept the fact therefore that some of the lesions in Lindau's Syndrome are not the results of an isolated antenatal developmental abnormality but that they represent a fundamental persistent lack of integration between blood vessels and parenchyma. One of the results is a proliferation of epithelial cells and one a proliferation of endothelial cells so that we

cannot say that the main fault lies predominantly with either. An exact counterpart to this disease lies in von Recklinghausen's neurofibromatosis in which the failure of integration lies between nervous and connective tissue.

SUMMARY

1. Three cases of Lindau's Syndrome among siblings are reported.

2. One patient died after removal of a cerebellar tumour and was found to have cysts in the lung, kidney and pancreas.

3. One died of renal carcinoma following successful removal of a cerebellar angioma.

4. One has had a successful removal of a cerebellar angioma.

5. The condition must be due to a hereditary but persistent abnormality in which there is a lack of integration between blood vessels and their field of supply. In the phase of foetal development this leads to cysts, in later life to neoplasms.

Note. Three of these patients were under the surgical care of Dr. K. G. McKenzie whom we wish to thank for the use of his records and for assistance in the preparation of this report. We are also indebted to Professor E. Linell for much assistance.

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SENSORY CHANGES WITH HERNIATED NUCLEUS PULPOSUS

LOYAL DAVIS, M.D., JOHN MARTIN, M.D., AND STANTON L. GOLDSTEIN, M.D.

Department of Surgery, Northwestern University Medical School, Chicago, Illinois

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IN RECENT years it has become common to perform surgery for herniations of the nucleus pulposus without myelographic verification, and many[1,2,4–10] believe that an accurate diagnosis can be made on clinical findings alone. In fact, Keegan[4–9] has devised a new dermatome chart based almost entirely on sensory changes in patients with herniated nucleus pulposus. In doing this he must assume that the majority of herniations involve only one nerve and are complete lesions, although he does note that in some instances there may be a lesser degree of compression, in which case, the

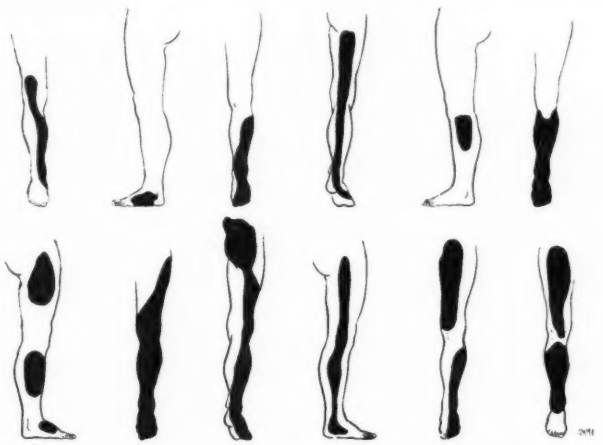

FIG. 1. Some of the variety of sensory patterns accompanying herniations of the nucleus pulposus at the L4–5 interspace.

localization may be misjudged. He states also that more than one nerve may be involved in a single herniation and that a more lateral, or more medial herniation than usual may be misleading.

On the basis of light pin scratch sensibility, Keegan has outlined dermatome areas for each of the posterior spinal nerve roots and states that the outlining of this so-called dermatome hypalgesia is diagnostic of single nerve involvement. Spurling and Grantham,[10] on the other hand, state that touch and temperature tests reveal sensory changes better than pin prick. They

also believe that myelography is not necessary in the majority of cases and that the level of the herniation can be diagnosed by sensory changes, but their sensory charts are different from those of Keegan. Falconer, Glasgow and Cole[3] describe sensory changes extending up the leg into the buttock, similar to, but not exactly like, Keegan's findings. However, they state that when the pain is severe, sensory impairment may become more extensive than can be explained on a segmental basis alone. They found extensive

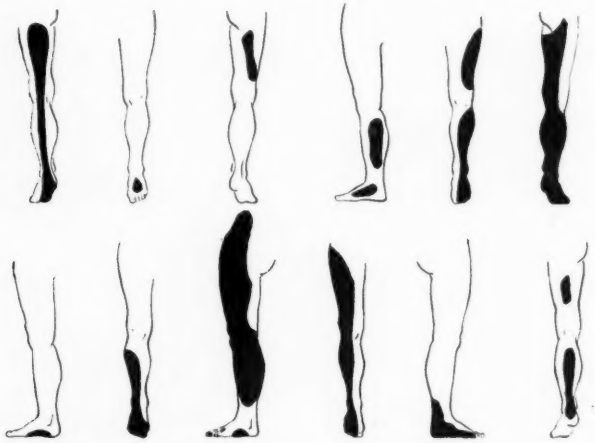

FIG. 2. Some of the variety of sensory patterns accompanying herniations of the nucleus pulposus at the L5–S1 interspace.

overlap, which Keegan did not find, and in several cases found a sensory loss confined to the foot and leg alone.

We have made a study of the sensory changes in 500 consecutive patients with surgically verified herniated nucleus pulposus. In all but 38, myelography was performed and the lesion verified. Eighteen of the herniations were in the cervical region, 201 at the L4-5 interspace, 234 at the L5-S1 interspace, and the remainder scattered at various levels throughout the spinal column or in multiple locations. Of the 500 patients, 327 had demonstrable sensory changes, which were extremely variable. Herniations at the L4-5 interspace alone produced 38 different patterns of sensory involvement varying from a small area of diminished sensation on the lateral aspect of the calf to hypalgesia of the entire thigh, leg, and foot (Fig. 1). Herniations at the L5-S1 interspace produced 29 different sensory patterns (Fig. 2).

It was interesting and significant to note the variability of the sensory findings with each particular examiner. These examinations were done by the authors and 6 other neurosurgical fellows and comparisons made. Pin prick and light pin scratch stimuli were used. The results also depend to some extent upon the patient's intelligence, suggestibility and psychic makeup.

These variable factors mitigate greatly against accurate localization of the level of the lesion by sensory loss alone.

Of the 201 patients with herniated nucleus pulposus at the L4-5 interspace, only 138 had demonstrable sensory changes. Of these, 21 had sensory diminution involving the posterolateral aspect of the thigh and/or the calf; 51 had involvement of the posterolateral aspect of the thigh and/or the calf plus the dorsolateral aspect of the foot, while in 13 patients it was limited

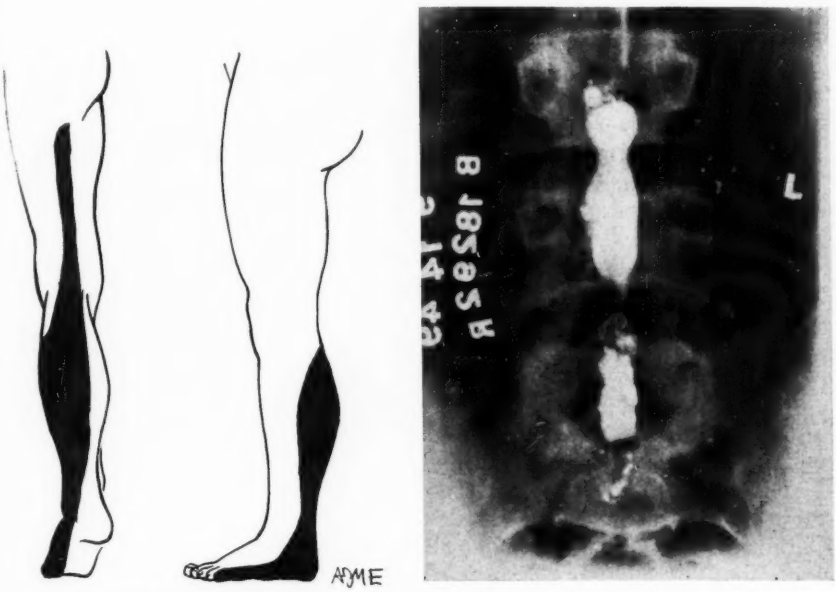

FIG. 3. Although the sensory changes would seem to indicate a herniation of the nucleus pulposus at the L5–S1 interspace (1st sacral root), myelography showed the lesion to be at the L4–5 interspace. This was later verified at surgery.

to the dorsolateral aspect of the foot only. Seven patients had sensory changes on the anterior aspect of the thigh, leg and/or the dorsum of the foot, and 6 had involvement of the entire thigh, calf and/or foot. Five had bilateral involvement. The sensory changes in the remaining 37 patients were evenly distributed between other miscellaneous areas and did not fall into any of the categories mentioned above. No typical sensory pattern could be demonstrated for herniations at the L4-5 interspace. In fact, the sensory changes were often misleading. For example, one patient had hypesthesia and hypalgesia extending in a narrow band along the posterior aspect of the thigh, the posterolateral aspect of the calf and the lateral aspect of the foot, including the little toe, corresponding most closely to the diagnosis of a herniation at the L5-S1 interspace, involving the posterior root of the 1st

sacral nerve, according to Keegan's dermatome chart and to the conception of many investigators. Yet, myelography revealed an almost complete block at the L4-5 interspace, and at surgery a herniation of the nucleus pulposus between the 4th and 5th lumbar vertebrae was found (Fig. 3).

Likewise, herniations at the L5-S1 interspace produced no typical pattern, and herniations at these two levels could not be differentiated on the basis of sensory changes alone. Of the 234 patients with herniated nucleus pulposus at the L5-S1 interspace, only 148 had demonstrable sensory changes. Of these, 18 had sensory diminution involving the posterolateral aspect of the thigh and/or the calf, 68 had involvement of the posterolateral aspect of the thigh and/or the calf plus the dorsolateral aspect of the foot, while in 29 patients it was limited to the dorsolateral aspect of the foot only. Three patients had sensory changes on the anterior aspect of the leg and foot, and 4 had involvement of the entire leg and foot. One had bilateral involvement. The sensory changes in the remaining 25 patients were located at various miscellaneous areas.

One patient had a herniated nucleus pulposus at the L1-2 interspace. This was a midline lesion producing sensory changes in both lower extremities. There were 10 patients with herniations at the L3-4 interspace and 5 had sensory changes. Two of these had hypalgesia involving the lateral aspect of the calf; 1, the lateral aspect of the thigh and calf; 1, the posterolateral aspect of the thigh and calf and the dorsolateral aspect of the foot, and 1 had bilateral involvement.

There were 16 patients with a transitional 1st sacral, or 6th lumbar, vertebra and they are considered separately. Fourteen had herniations at the L5-6 interspace. Five of these had no sensory changes, 7 had hypalgesia over the posterolateral aspect of the thigh and calf and/or the dorsolateral aspect of the foot, while 2 had changes limited to the lateral aspect of the foot only. Two patients had herniations at the L6-S1 interspace and both had sensory changes, one over the buttock, the posterior surface of the thigh and calf and the heel, the other over the lateral surface of the leg and dorsolateral aspect of the foot.

There were 20 patients who had multiple herniations verified at surgery: 3 at L3-4 and L4-5; 12 at L4-5 and L5-S1; 2 at L3-4 and L5-S1 and 2 at all three interspaces. Twelve of these patients had sensory changes, 7 having involvement of the posterolateral aspect of the thigh and calf and/or the dorsolateral aspect of the foot; 1, the dorsolateral aspect of the foot only; 2, the medial aspect of the leg and/or the foot; 1 had bilateral sensory changes and 1, the lateral aspect of the calf and medial aspect of the foot.

Of the 18 patients with herniated cervical nucleus pulposus, 12 had sensory changes. One patient had a lesion at the C3-4 interspace and had diminution of pin prick sensibility over the lateral aspect of the arm, forearm and hand. Nine patients had herniations at the C5-6 interspace and 7 of these had sensory changes. Three had hypalgesia on the lateral aspect of the hand and thumb only; 2, on the lateral aspect of the arm, forearm and hand;

1, on the lateral aspect of the forearm only, and 1, on the dorsal aspect of the arm and volar surface of the hand. There were 7 patients with herniated nucleus pulposus at the C6-7 interspace, and 3 of these had sensory changes:

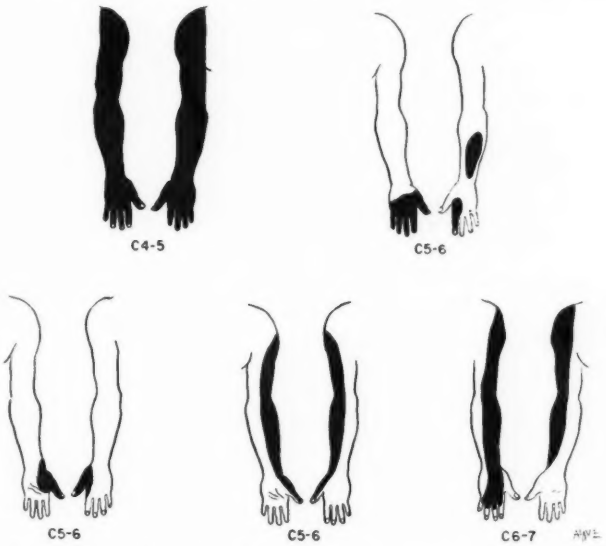

FIG. 4. Some of the variety of sensory patterns accompanying herniations of the nucleus pulposus at the cervical levels.

2 at the fingertips only and 1 on the lateral aspect of the arm, forearm and hand. Some of the sensory patterns with herniated cervical nucleus pulposus are shown in Fig. 4.

The extreme variability of sensory changes with herniated nucleus pulposus is readily understandable when one considers the fact that the lesions are almost never the same size or shape, nor in the same location, and may involve part of a posterior spinal root, an entire root, or more than one root, or may involve a root higher or lower than one would expect. Therefore, it appears to us not feasible to attempt to chart dermatomes from the study of patients with herniated nucleus pulposus.

With Keegan's scratch method, it was found that the sensory change was appreciated a little later than with pin prick, so that when the scratch was made from the hypalgesic area to the normal

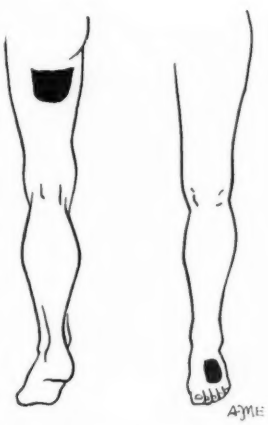

FIG. 5. Areas of sensory diminution after section of the 1st sacral root.

area, the extent of diminished sensation appeared to be slightly greater. However, it was not possible to demonstrate a narrow band of hypalgesia extending from the spine to the distal end of the extremity, as described by Keegan. In fact over half (198) of the patients with sensory changes had involvement of the distal part of the extremity only with no demonstrable sensory loss in the proximal portion.

Our experience with section of a single posterior spinal root in the lumbosacral area is limited. A patient who had a neurofibroma of the 1st sacral roots had a division of the roots to remove the tumor and the only demonstrable sensory changes were slight hypalgesia over the posterior aspect of the upper thigh and a small area of hypalgesia on the dorsum of the foot (Fig. 5). This is explained undoubtedly by a sensory overlap of adjacent uninjured posterior spinal roots.

SUMMARY

Sensory changes in 500 patients with herniated nucleus pulposus showed no correlation between the sensory pattern and the level of the lesion. The extreme variability in the sensory pattern makes the method of devising a dermatome chart from the sensory changes in patients with herniated nucleus pulposus an unreliable one. While myelography is not necessary to establish the diagnosis of a herniated nucleus pulposus, we believe it is the most reliable method of localizing the lesion in the lumbar spine.

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CHORDOMA: EXPERIENCE WITH THIRTEEN CASES

JAMES L. POPPEN, M.D., AND ARTHUR B. KING, M.D.*
Department of Neurosurgery, The Lahey Clinic, Boston, Massachusetts

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IT HAS been nearly a century since slimy, sessile tumors on the clivus blumenbachii were first recognized. For fifty years, it has been established that these neoplasms originated from remnants of the embryonic chorda dorsalis. Since then, tumors of this tissue have been described arising along the entire axis (Fig. 1) of the chorda from the sphenoid region to the coccyx. When fragments became isolated chordomas were found in unusual

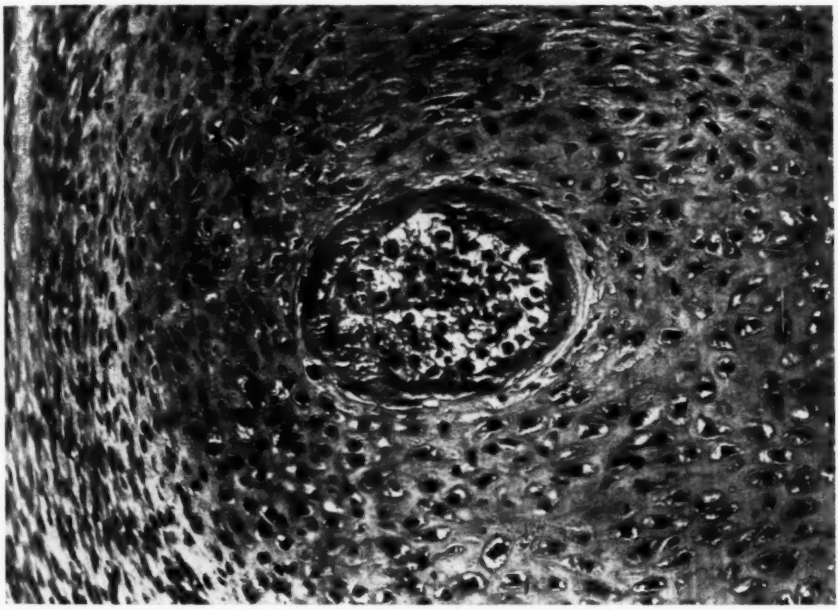


FIG. 1. Notochord in a 3 cm. human fetus. Note similarity to the photomicrographs of the tumors in this series.

positions, such as the alveolar process of the mandible, the maxilla, tonsillar region and superior portion of the occipital bone.[8]

Chordomas that produce clinical symptoms are rare and up to the present time only about 300 cases have been reported. Most studies on the subject have been based on one or at best a few cases. We have had experience with 13 cases. At the Lahey Clinic, about 1800 cases of neoplasm affecting

* Formerly Neurosurgeon to The Lahey Clinic; now head of Neurological Surgical Section, Guthrie Clinic, Sayre, Pennsylvania.

the central nervous system have been verified, making the incidence of chordomas less than 1 per cent in a large series. For details of incidence, of embryology, and location and pathology, many excellent reviews are available.[1,3,4,5,8]

For purposes of description, chordomas can be grouped as intracranial and those arising in the spine. We encountered 7 of the former and 6 of the latter. A brief clinical résumé, together with roentgenologic findings and a short pathologic description, will be given.

INTRACRANIAL TUMORS

Case 1. A man, aged 64 years, had noticed a left visual field defect 1 year before admission. This defect gradually increased to a temporal hemianopsia. Since the age of 12 years he had been nearly blind in the right eye as a result of chorioretinitis. A course of roentgen therapy to the pituitary region was given elsewhere. At first he appeared to respond favorably but later the visual failure progressed. A short time before admission, sudden episodes of unconsciousness, lasting 2 to 3 minutes, preceded by a vague, nonlocalizing aura, made their appearance. Headaches also became prominent.

Examination disclosed primary optic atrophy. The vision was restricted to a small binasal field.

FIG. 2. *Case 1.* Photomicrograph of tumor.

The original roentgenograms indicated a ballooning of the sella and destruction of the anterior clinoid processes, consistent with a pituitary adenoma.

Operation (by J. L. P.). A brownish-red tumor was found lying between the optic nerves. The neoplasm extended posteriorly to the pons and laterally under both temporal lobes. A large mass of necrotic-appearing tissue was excised, but only part of the neoplasm could be removed. The patient died a few days after operation.

Autopsy revealed a cauliflower mass, 4×3×1 cm., extending from the chiasm

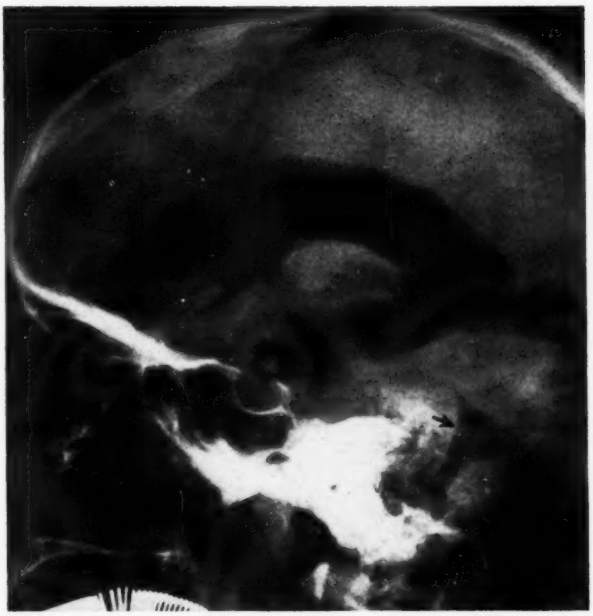


FIG. 3. *Case 2.* Ventriculogram, lateral view. The posterior bowing and displacement of the 4th ventricle are suggestive of an intrapontine tumor.

to the interpeduncular cistern, and along the left side of the pons. It had a smooth surface, but was firmly fixed to the chiasm and surrounding dura. The tumor had eroded the base of the sella, filled the sphenoid sinus and projected into the nasopharynx. No remnants of the pituitary gland were found.

Microscopic Examination. The tissue was bizarre and variable. Some areas were composed of spindle cells of varying size, arranged in strands, with fairly abundant cytoplasm. The cells were scattered in an eosinophilic hyaline matrix. Foci of large, irregular, round to polygonal cells with indistinct boundaries and pale, finely granular, moderately eosinophilic cytoplasm were seen. These cells had large, vesicular nuclei, and several had prominent nucleoli. Many cells were vacuolated and contained mucin-like material. Mitoses were rare. The tumor included well-formed bony trabeculae, showing both resorption and slight osteoid formation (Fig. 2).

Case 2. A woman, aged 26 years, had had "fainting spells," sometimes accompanied by nausea and vomiting, for 4 years before coming to the clinic. Definite convulsions were not noted. At another hospital lumbar puncture demonstrated that the spinal pressure was elevated; the fluid was normal. Suboccipital exploration carried out elsewhere was negative. This was followed by severe suboccipital headaches, nausea, vomiting and progressive weakness of the left arm and leg.

Examination. The pupils were large and reacted to light. Papilledema, about 1 D., was present in each eye. A pronounced palsy of the left 6th nerve was present. There was a questionable peripheral weakness of the left 7th nerve and considerable weakness, hypotonus and ataxia of the left arm and leg. All tendon reflexes were

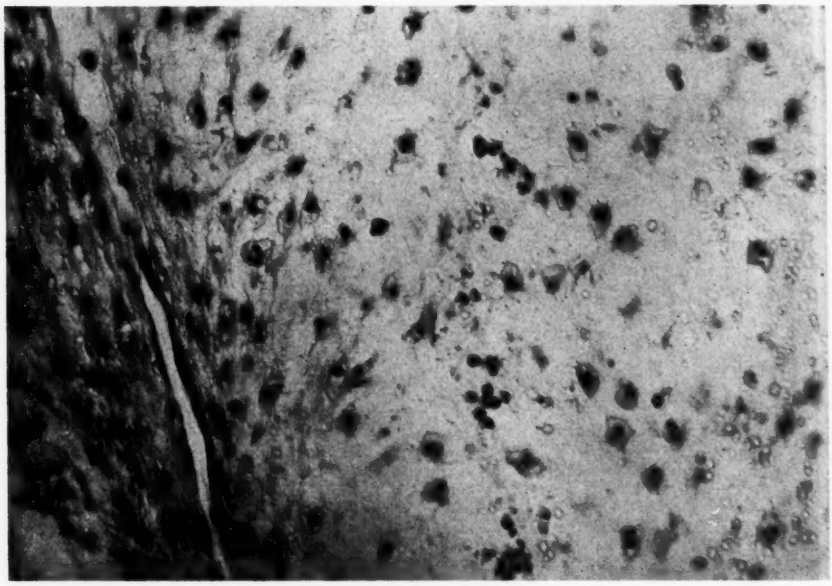


FIG. 4. *Case 2.* Photomicrograph of tumor.

hyperactive, more so on the left than on the right. Patellar and ankle clonus was demonstrated in the left leg.

A ventriculogram showed symmetrical dilatation of the lateral and 3rd ventricles. The 4th ventricle was pushed upward and backward. The aqueduct of Sylvius was displaced upward in a gentle curve, suggesting a glioma of the pons (Fig. 3).

Operation (by J.L.P.). Exploration of the posterior fossa was done immediately. A large tumor, resembling raspberry jelly, was found under the pons and medulla. After aspiration of much of its contents the neoplasm was found to extend under the pons to the right side, anteriorly under the incisura, and along the basisphenoid. Part of it lay under the 7th and 8th nerves, and another portion projected into the jugular foramen. The tumor appeared to be encapsulated. The pons was reduced to a ribbon. After a long and unsatisfactory postoperative course, the patient died.

Autopsy showed small bits of tumor in the sphenoid sinus and in the petrous portion of the left temporal lobe.

Microscopic Examination. The tumor was composed of cells forming broad irregular sheets. They were roughly stellate in shape with relatively large and clear spaces between them. The cellular cytoplasm was often clear, but sometimes vacuolated in appearance. In several places the bone was eroded and neoplastic cells were found in the trabeculae. Mitoses were rare (Fig. 4).

Case 3. A woman, aged 34 years, complained of tinnitus in the right ear for 3 years. Two years before admission she discovered that the hearing in that ear was diminishing. Attacks of "dizziness" began about 1½ years before admission, and

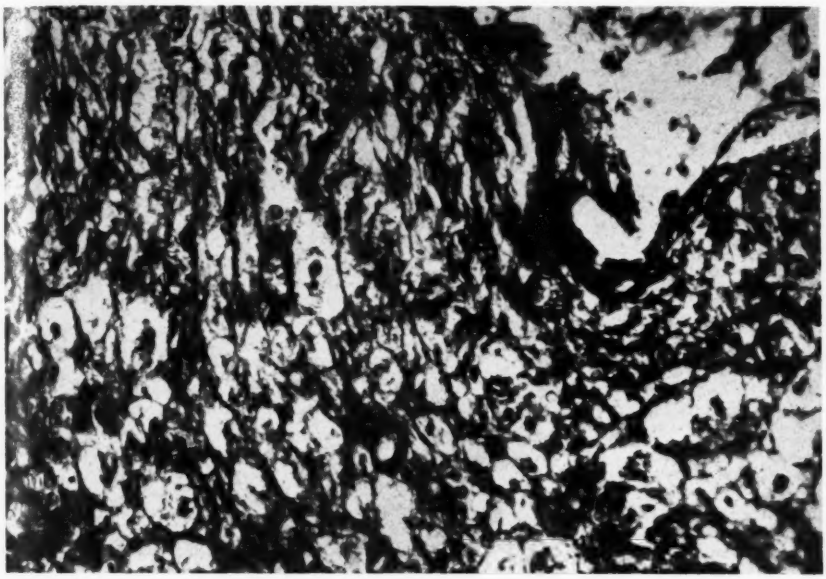


FIG 5. *Case 3.* Photomicrograph of tumor.

they were followed by an unsteady gait and hoarseness. About this time the right side of the face became "numb." For many years she had suffered from headaches but they had become more severe and intense recently and she felt "dopey."

Examination. The patient was alert and cooperative. A coarse nystagmus on looking to the right was noted. There was partial to complete paresis of the 5th, 7th, 8th, 9th, 10th, 11th and 12th cranial nerves on the right. The right arm and leg were markedly ataxic. The patient fell to the right in the Romberg test.

Roentgenograms of the skull showed thinning of the medial inferior portion of the right petrous ridge, with some bony erosion. The clivus was notched. The destruction was somewhat greater than usually seen with an acoustic tumor.

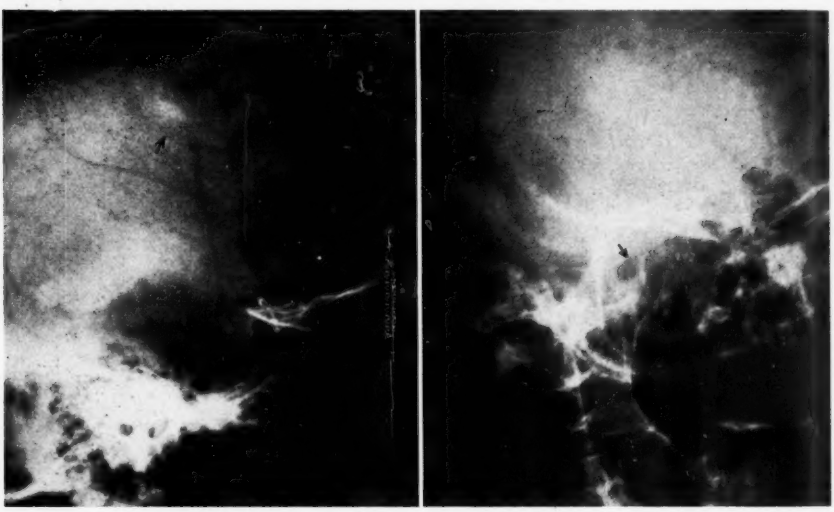
Operation (by J.L.P.). A tumor suspected of being an acoustic neuroma was found. None of the cranial nerves, however, was adherent to the tumor, and there was more than the usual amount of bony erosion at the porus acusticus. So much

of the bone was eroded by tumor that the eustachian tube could be palpated.

Microscopic Examination. The cellular pattern of the tumor was typical of a well differentiated chordoma (Fig. 5).

Course. Two years after operation there was sudden onset of diplopia. There was slight ptosis of the left eyelid and paralysis of the right 6th nerve. The right 5th nerve was intact. Four years after operation a right abducens palsy was present; the palate appeared to move well but she had difficulty in swallowing. The right side of the tongue was atrophied. The gait was ataxic. The patient died at home 6 years after operation, probably from recurrence.

Case 4. A woman, aged 68 years, 3 years before admission found, on awakening, that her right eye had "turned in." She complained of severe throbbing headache in the vertex. The strabismus persisted for 5 months when the right eyelid began



FIGS. 6 and 7. *Case 4.* Roentgenograms. (Left) Lateral view. Upper arrow points to meningioma; lower arrow to region of eroded posterior clinoids. (*Right*) Demonstrating enlargement of right optic foramen.

to droop and finally closed. It remained shut for several months when it spontaneously began to reopen and the strabismus was lost (3rd and 6th nerve palsy?).

The vision became progressively impaired and 2 months before admission the right lid again closed. A few days later the left lid closed and the vertex headaches recurred. This situation lasted for several weeks when once more the left eye began to open and shortly before she came to the clinic the right lid could be elevated slightly. Vision, however, diminished greatly; it was slightly better on the right than on the left.

For some time her legs had become increasingly weak so that she was unable to walk without assistance. Shortly afterward the fluid intake and urinary output increased. She lost 25 lbs. in weight because of loss of appetite.

Examination. The patient was alert and cooperative. The sense of smell was

intact. Vision was 20/400 on the right and restricted to hand movements on the left. Both optic disks showed marked primary optic atrophy. There was ptosis of the right lid. The right pupil was larger than the left. Neither pupil reacted to light. There was a weakness of all eye movements on the right, most marked in the upward gaze. The left eye was in lateral deviation, with only a weak medial and downward movement. The inability to walk appeared to be due to generalized weakness.

Roentgenograms of the skull showed an area of calcification suggesting a parasagittal meningioma in the falx in the parietal region, more pronounced on the left. The sella was destroyed (Fig. 6). The right orbital roof was thinned and the

FIG. 8. *Case 4.* Photomicrograph of tumor.

optic foramen eroded (Fig. 7). Both posterior clinoids were absent. The left anterior clinoid was sharpened and pushed upward. The sphenoid sinus was eroded and partially filled with a mass. The basisphenoid was also eroded, particularly on the right.

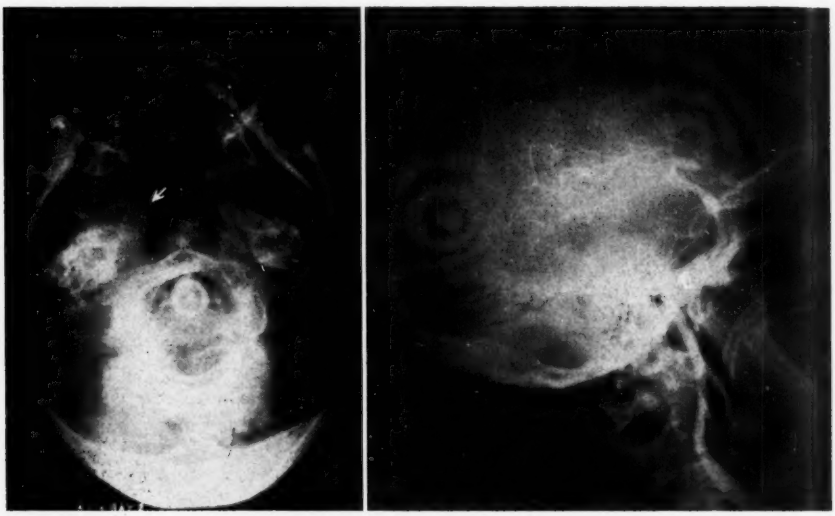
Bilateral carotid arteriograms were normal.

Operation (by J.L.P.). A left craniotomy was done, and a dumbbell-shaped meningioma was found in the falx, just anterior to the motor area. This was easily removed but its presence did not explain the roentgenologic changes or clinical findings and for that reason the chiasm was immediately explored. The chiasm appeared normal, and there was no tumor beneath it. The postoperative course was stormy and the patient died 8 days later.

Autopsy. There was a large reddish tumor, 3×2.5×1.5 cm., in the sphenoid sinus and in the sella. It did not push through the diaphragm of the sella or the dura. It appeared to be encapsulated. It extended anteriorly, however, and impinged on the optic and extra-ocular nerves as they entered the orbit, causing a flattening and distortion. It surrounded the carotid arteries but did not displace them.

Microscopic Examination. The sections were characteristic of a chordoma (Fig. 8). They suggested only a low-grade malignancy, despite the local invasion of bone.

Case 5. A woman, aged 51 years, had had a sudden episode of diplopia 7 years before coming to the clinic. The right eye turned in (6th nerve palsy?). Roentgeno-



FIGS. 9 and 10. *Case 5.* (*Left*) Roentgenogram of base of skull demonstrating erosion of bone; arrow points to medial shadow outlining tumor. (*Right*) Arteriogram, showing marked forward and upward displacement of the internal carotid artery.

grams of skull and the spinal fluid at that time were said to be normal. No specific therapy was instituted. Over a period of some months, the paralysis disappeared.

She remained well until 2 years before admission. At that time a pelvic operation was performed. A few days after this, the right eye closed, the eye turned in and the right side of the face became anesthetic. The right arm became weak at the shoulder. Within a short period, dysphagia and dysarthria appeared. Recently she began to feel unsteady on walking, and tended to deviate to the left.

Examination. The patient was anosmic on the right. The right optic disk showed advanced primary optic atrophy. Vision was impaired, but to gross tests the visual fields were not restricted. The right eyelid drooped. The right pupil measured 3 mm. and the left 5 mm. The right pupil reacted sluggishly both directly and consensually to light. The entire right side of the face was hypesthetic and the corneal reflexes were absent. Medial movement of the right eye was limited to the midline. The 7th and 8th nerves were intact; however, the 9th, 10th, 11th and 12th nerves

were completely paralyzed on the right. None of the cranial nerves on the left was involved. Marked weakness and spasticity of the left arm and leg were noted, with increased tendon reflexes.

Roentgenograms of the skull showed erosion of the dorsum sellae, with complete destruction of the right anterior clinoid process and the lesser wing of the sphenoid bone. The floor of the middle fossa was eroded in the region of the foramina spinosum ovale and lacerum (Fig. 9). On the right the clivus, basisphenoid and petrous ridge showed evidence of destruction. The clivus was displaced forward, and the sphenoid sinus was filled by a tumor mass.

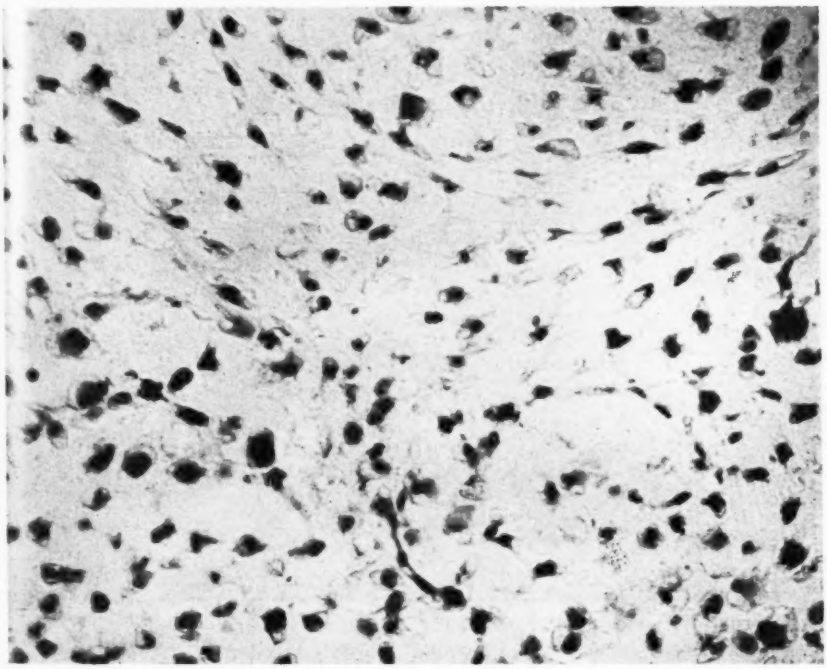


FIG. 11. *Case 5.* Photomicrograph of tumor.

An arteriogram showed pronounced distortion of the course of the right internal carotid artery (Fig. 10). It was straightened and pushed forward. In the antero-posterior projection, the middle cerebral artery was pushed medially and upward, indicating a large middle fossa tumor.

The nose and throat examination revealed a large submucosal mass in the right fossa of Rosenmüller.

Operation (by J.L.P.). A huge extradural tumor was found in the middle fossa. It had eroded the entire floor and projected into the nasopharynx. There was an extension into the posterior fossa anterior to the pons. The tumor surrounded the internal carotid artery throughout its extracranial and intracranial course. It was

composed of yellow slimy mucoid material. The bulk of the mass could be readily aspirated.

Microscopic Diagnosis. Typical chordoma (Fig. 11).

Course. Postoperative meningitis developed and the patient died 2 months later. Postmortem examination was refused.

Case 6. A man, aged 51 years, had a dull, left-sided headache 4 or 5 years before admission. This was soon followed by attacks of "dizziness," lasting 2 to 48 hours, which occurred 2 to 3 times a week. Hearing in the left ear was lost within 3 weeks.

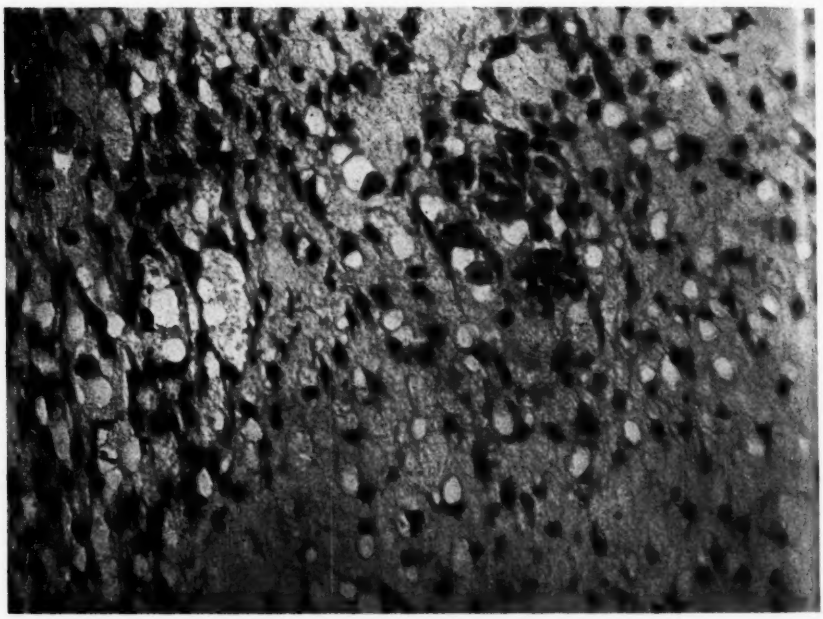


FIG. 12. *Case 6.* Photomicrograph of tumor.

Unsteadiness was noted, with a tendency to fall to the left. Within the last year, there had been two attacks of syncope.

Examination. A coarse nystagmus on looking to the left was noted. The left corneal reflex was diminished, the left ear was deaf and vestibular responses were absent. There was atrophy of the left occipital muscle group, the sternocleidomastoid muscle and of the left side of the tongue. Mild ataxia of the left arm and leg was recorded and Romberg's sign demonstrated falling to the left.

Spinal fluid pressure was normal; total protein 36 mg. Roentgenograms of the skull were normal. Diagnosis: tumor of the cerebellopontile angle.

Operation (by J.L.P.). A large encapsulated tumor was found in the region of the foramen magnum and along the floor of the left occipital bone. All the cranial nerves were displaced upward and laterally by a smooth-surfaced tumor lying anterior to the pons. Upon opening the capsule, a gelatinous, currant jelly-like material was readily aspirated. The remaining firm portion of the tumor was easily

removed. It had caused pressure erosion of the occipital bone. All the cranial nerves were saved. A projecting cone of tumor was also shelled out of a nest made by it in the anterior surface of the medulla.

Microscopic Examination. The tumor showed a cellular pattern typical of a chordoma. The cells were large and well formed. No mitoses were seen (Fig. 12).

Postoperative course was uneventful. The patient returned to work at the end of 3 months. When seen 5 years later for a check-up examination, he showed remarkably few deficits. The left ear was deaf, the left trapezius was weak and the left side of the tongue atrophied. The ataxia had disappeared and the Romberg's sign was steady. A slow coarse nystagmus on left lateral gaze was still present.

Case 7. A man, aged 59 years, noticed failing vision of the right eye in June 1948, associated with failing memory and euphoria of gradual onset. The symptoms were progressive and additive, with onset of headache, mental confusion, inability to concentrate, confabulation, drowsiness, diminution in sexual power, lack of usual inhibitions, and paranoid tendencies. In September 1949 roentgenograms demonstrated complete atrophy of the posterior clinoids and marked atrophy of the dorsum sellae. The region of the clivus showed widening with irregularity and atrophy extending to the mastoids. The clinical diagnosis was tumor occupying the central portion of the 3rd ventricle and arising from the base of the skull. Ventriculograms at that time performed elsewhere demonstrated no defect in the ventricular system. He was treated with radiation, without improvement. The patient was admitted to the clinic on Feb. 27, 1950.

Examination. He was well-nourished, somewhat overweight, euphoric and garrulous. Both optic disks were pale; right homonymous hemianopsia was found. There was marked diminution in visual acuity, more so on the left. Spinal fluid pressure was 210 mm.; total protein 97 mg.

On Feb. 28, 1950, oxygen-encephalography and bilateral carotid arteriography were done. The ventricular system was moderately and symmetrically dilated. The 3rd ventricle was well filled; a large mass projected upward into its anterior portion, displacing the foramen of Monro posteriorly. The aqueduct of Sylvius and the 4th ventricle were well filled and appeared normal. A large mottled mass of bone could be seen arising from the basisphenoid; it was apparently related to the soft tissue mass extending into the 3rd ventricle. The carotid arteriograms were not helpful except to rule out a large aneurysm.

Operation. Craniotomy was performed in the frontal region. The tumor was identified behind the chiasm, pushing upward into the 3rd ventricle. The entire tumor was removed with the exception of a few bits that were left attached to the left internal carotid artery and the anterior clinoid.

The patient died on the 3rd postoperative day.

Autopsy. The entire pituitary gland and surrounding bony structures were firmly encased in dark red cartilaginous tissue continuous with the adjacent sphenoid bone. There was considerable edema in the region of the hypothalamus and midbrain. Moderate cardiac dilatation, pericardial effusion, bilateral bronchopneumonia and coronary sclerosis were present.

Microscopic Diagnosis. Chordoma (Fig. 13).

Discussion. As has been pointed out by others, these neoplasms may begin anywhere along the midline of the base of the skull. Because of the ease with which they erode bone, they tend to spread out in all directions.

Clinically, they may seem to be on one side, but at operation or autopsy they are usually found on both sides of the midline, although predominantly the mass may be much larger on one side. The dura does not appear to be a great barrier, and the tumor invades the intracranial cavity either by direct extension or along the cranial nerves. Likewise, it may extend into the sphenoid sinus, nasopharynx, middle ear and even into the jugular foramen.

Although these neoplasms show considerable histologic variation and certainly their rate of growth is variable, in the cases in which there is

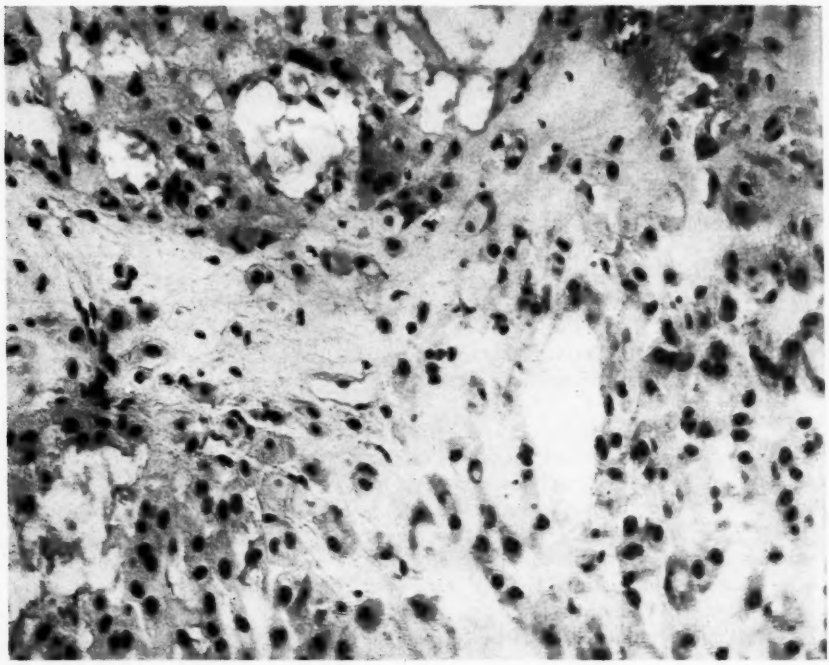


FIG. 13. *Case 7.* Photomicrograph of tumor.

rapid progression of symptoms, such changes as marked anaplasia, tumor giant cells and many mitoses that are ordinarily associated with a high grade of malignancy are not seen. Metastases were not found in any of our cases, although these have been reported in the literature.[10] Godtfredsen believed that the degree of malignancy could not be told from histologic sections alone and this is certainly our experience.

In an analysis of 25 cases with intracranial signs, Godtfredsen thought that the initial symptoms fell into two groups: (a) those involving the eye

(middle fossa), and (b) those of generalized cerebral hypertension. In 3 of our cases the symptoms suggested a lesion of the posterior fossa, in 2 being rather typical of an acoustic neuroma. Givner[6] stated that the four most common symptoms were headache, visual disturbances, nasal obstruction and pain in the neck. In our small series, these symptoms were not common.

As previously noted, there was erosion of bone to a greater or lesser extent in all our cases. Symptoms resulting from nerve paralysis, however, appear to be due to compression. The onset is often slow and progressive, although on occasions symptoms have appeared so abruptly as to suggest the presence of an aneurysm. Sudden hemorrhage within the neoplasm is probably the explanation.

Although the progression of symptoms is often almost identical with that of nasopharyngeal carcinoma, we have been impressed with the fact that pain is not nearly so common or as severe, when present, as in patients with cancer. Lymphadenopathy in the neck, which is commonly found in cases of cancer, is rarely seen with chordomas.

Case 1 had symptoms and signs almost identical with those of a pituitary tumor. The episodes of unconsciousness and headache were late manifestations. This could well be true of a pituitary adenoma which had broken through the capsular wall. Signs of pituitary dysfunction were not prominent, but this is likewise true of many chromophobe adenomas.

Case 4 showed a more confusing picture. The signs and symptoms suggested bilateral intracranial aneurysms. This diagnosis was confused by the roentgenologic findings of a parasagittal meningioma and "normal" arteriograms. The destruction about the sella was never fully evaluated, but suggested to one of us (A.B.K.) a carcinoma of the pituitary.

The illness in Case 5 started with transient 6th nerve palsy; then 5 years later a series of cranial nerve palsies developed on the right side, starting with ptosis of the eyelid (3rd nerve). By the time the patient came to the clinic, all the cranial nerves on the right were involved except the 7th and 8th. When the marked destruction of the base of the skull was found on roentgenologic examination, we felt certain we were dealing with a carcinoma of the nasopharynx. The otolaryngologist, however, was positive that the mass was pushing into the nasopharynx from the skull, rather than vice versa.

Cases 3 and 6 seemed typical of a tumor of the cerebellopontile angle; apparently there is nothing to distinguish them, from a clinical viewpoint, from an acoustic neuroma. Only the roentgenogram in Case 3 suggested a condition more malignant than the usual acoustic neuroma. Case 2 is peculiar in that, by the time the patient was seen, the picture of a glioma of the pons was present. All the early symptoms were those of increased intracranial pressure which admittedly is unusual for a chordoma. Later the injury to the cranial nerves in the posterior fossa and the "characteristic" ventriculogram made the diagnosis of pontine glioma seem more positive. The tumor had invaded and replaced most of the pons and midbrain so that we are

unable to point out any clinical signs that are strikingly different from those of a pontine glioma.

To summarize, chordomas should be considered when dealing with any neoplasm at the base of the brain or in the nasopharynx. Bone destruction which is at all marked makes the possibility of a chordoma greater. Even nasopharyngeal carcinomas may not produce marked bony erosions. There does not appear to be a characteristic syndrome and many other types of neoplasms may be simulated.

The only treatment appears to be surgical removal. Of 7 patients, only 2 survived the immediate postoperative period. One lived for 6 years. The other is alive and well 5 years after operation.

The extensiveness of the tumor by the time most patients are seen, together with its early bony invasion, makes total extirpation the exception rather than the rule. This has been a general finding. We have had no experience with roentgen therapy, but Case 1 suggests that at least the ordinary form applied to pituitary tumors is unsatisfactory.

CHORDOMAS ARISING IN THE SPINE

Cervical Region. We have encountered 6 cases in which chordomas have arisen in the spine. In 3 the chordomas were in the cervical region and in 3 in the lumbar or sacral region. In an additional case in which operation was performed by one of us (J.L.P.), the tumor probably was a chordoma, certainly it appeared so clinically, but when the neoplasm was studied microscopically, it was so difficult to classify that this case was not included in this series.

All of the patients showed marked neurologic signs and involvement of bone on roentgenologic examination. In none of the cases was a correct diagnosis made preoperatively as to type of neoplasm; most of them were thought to be metastatic carcinoma.

Case 8. A woman, aged 53 years, was first seen in October 1947, with the history of gradually progressive stiffness of the neck, together with pain which extended down the left arm to the hand. Shortly after the onset of the pain, weakness was noticed in the arm, and this too had progressed so that for 2 weeks all voluntary motion had been lost. Three months before admission she noticed a feeling of strangulation when she swallowed. For 1 month there had been progressive weakness of the right arm. Excessive sweating had been present over the face for a week. A few days before admission a lumbar puncture was done. Immediately afterward, profound weakness of the left leg, a "pressing" sensation in the chest and complete paralysis of the bowel and bladder occurred.

Examination. There was profuse sweating about the face; the remainder of the body was dry. The neck was stiff because of muscle spasms but it could be moved both actively and passively. There was almost complete quadriplegia, only slight finger movements remaining in the hands, and no motion in the lower extremities. All tendon reflexes were markedly hyperactive. The Babinski responses were positive, and clonus was present in both ankles. There was a pronounced sensory level to pain at the 4th cervical vertebra. Vibratory sense was absent in the legs but still

poorly appreciated in the hands. Position sense was present in the legs but absent in the arms.

Roentgenologic studies of the cervical spine disclosed bony erosion of the 4th cervical vertebra. The pedicles on the left side were destroyed and there was a smooth, round defect in the body. Involvement of the 3rd cervical vertebra by the destructive process was equivocal.

Operation (by J.L.P.). A bluish extradural tumor was found involving the laminae of the 3rd and 4th cervical vertebrae. It was situated principally on the left side of the cord, compressing it to the right. The underlying vertebra was involved by the neoplasm. The tumor was soft and gelatinous. It was thought that most of it was removed. In order to determine the extent of the tumor, roots at the 2nd and 3rd cervical vertebrae on the left were divided.

Microscopic Studies. The tumor proved to be a typical chordoma (Fig. 14).

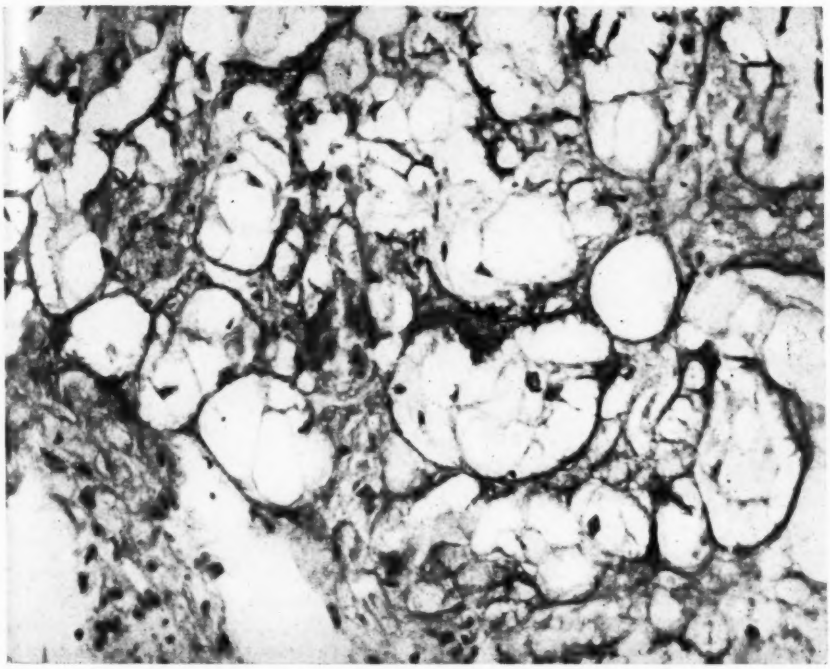


FIG. 14. *Case 8.* Photomicrograph of tumor.

Postoperative course was uneventful. Motor power returned fully, as did sensation, except for the area supplied by the two roots that were sectioned.

When the patient was seen again in April 1948, the weakness in the left arm and choking sensation in the throat had returned. A large, firm, fixed, nontender mass was found in the neck, bulging into the posterior pharynx. Roentgenograms of the neck disclosed a large soft tissue mass in the nasopharynx. The defect in the 4th cervical vertebra appeared to be larger and the bony destruction was advancing

slowly. Roentgen therapy was begun and a month later the tumor was reduced to half its previous size and some strength had returned in the left arm.

On examination in September 1949, the mass had resolved, strength in the left arm was normal and the patient had no specific complaints. Roentgenograms showed that the soft tissue mass had almost disappeared.

Despite x-ray therapy, the disability continued to increase. On re-exploration no evidence of tumor was apparent. The cervical cord was compressed by disuse, scar tissue and possibly by changes resulting from roentgen therapy. The patient's condition improved following the decompression.

Case 9. A man, aged 30 years, when seen in October 1942 stated that for 10 months he had been bothered by numbness of his back and extremities. The numb-

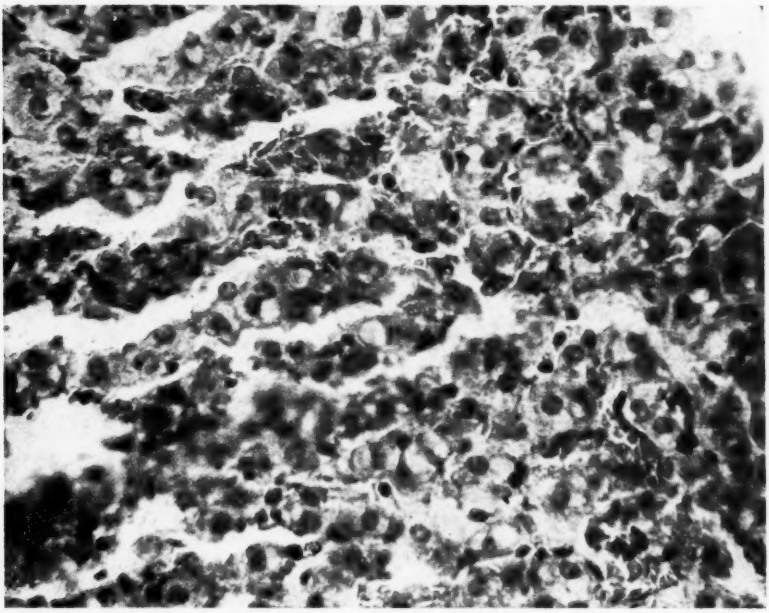


FIG. 15. *Case 9.* Photomicrograph of tumor.

ness had started in the fingertips and later spread to involve the arms, trunk and finally the legs. For some time paresthesias had been present, and when he touched something cold, he felt as though it were "burning." Recently he had had difficulty in walking, his thighs felt "heavy" and he had to "push" his legs along. Also he had been markedly constipated and had been catheterizing himself.

Examination. There was mild weakness of plantar flexion of both feet. All the tendon reflexes were hyperactive. Abdominal and cremasteric reflexes were absent. There were positive Hoffmann's responses in both hands, bilateral ankle clonus and bilateral extensor plantar responses. A definite sensory level to all modalities was present at the level of the 6th cervical vertebra.

Lumbar puncture demonstrated a spinal fluid block. A myelogram revealed a complete block at the 5th cervical vertebra.

Roentgenograms of the cervical spine suggested the presence of an osteoblastic malignancy.

Operation (by J.L.P.). An extradural tumor was found anteriorly at the 5th cervical vertebra. The tumor had a cartilaginous appearance. Practically the whole body of the vertebra was involved. Most of it was curetted away.

Microscopic Examination. The tissue resembled fetal cartilage (Fig. 15). Many of the cells were large and vacuolated. It was our opinion that this was a chordoma resembling the condition seen in early fetal life.

FIG. 16. *Case 9.* Lateral roentgenogram showing 5th cervical vertebra largely replaced by osteoblastic tissue 6 years after surgery.

FIG. 17. *Case 10.* Lateral roentgenogram demonstrating posterior central destruction of 6th cervical vertebra with osteoblastic changes in the anterior and inferior portion.

Postoperative course was uneventful. All the neurologic signs disappeared. In February 1948, roentgenograms of the cervical spine revealed that the 5th cervical vertebra was largely replaced by osteoblastic tissue with no collapse (Fig. 16). When the patient was last heard from in March 1951, there was no clinical evidence of recurrence.

Case 10. A woman, aged 60 years, with poorly controlled diabetes, was first seen in January 1949. She had used cathartics for 50 years but 6 months before admission, and despite taking these cathartics, she became more constipated; her abdomen became distended and felt "stiff." About this time weakness of the legs became apparent and progressed so that she could walk only with support.

Examination. General muscular wasting was noted, which was most marked in the forearms and hands. A few fibrillations were seen. Tendon reflexes were absent

in the arms but were hyperactive in the legs. Both plantar reflexes were extensor. No sensory changes could be demonstrated.

Roentgenograms of the cervical spine showed the pedicles spread at the 6th and 7th cervical vertebrae. The body of the 6th vertebra was partially destroyed (Fig. 17). The laminae of the 5th cervical vertebra were involved by the destructive process. The roentgenologic findings seemed characteristic of metastatic carcinoma.

Spinal fluid pressure was 120 mm., with normal dynamics; total protein 254 mg. A myelogram revealed a complete block at the 6th cervical vertebra.

Operation (by A.B.K.). The laminae of the 6th and 7th cervical vertebrae were infiltrated by a neoplasm. A reddish, meaty, extradural tumor that encircled the

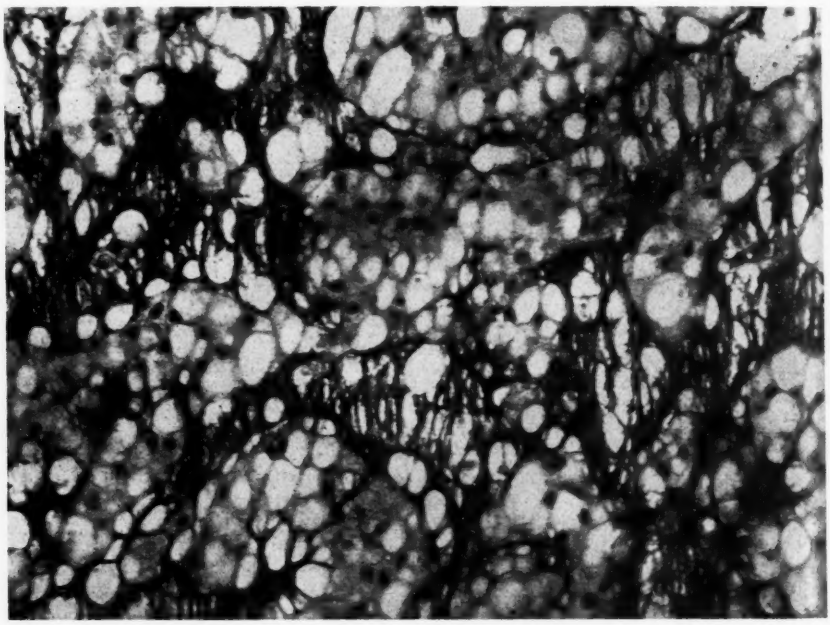


FIG. 18. *Case 10.* Photomicrograph of tumor.

cord was uncovered. When this was removed, it was found that the bodies of the 6th and 7th cervical vertebrae were almost destroyed by the tumor. All available tumor tissue was removed. There was no intradural extension.

Microscopic Diagnosis. Chordoma (Fig. 18).

Postoperative course was uneventful. Pain in the arms was lessened and there was partial return of strength to the extremities. Constipation remained a problem.

About 2 months after operation, recovery ceased and symptoms of cord compression recurred. A second hospital admission was arranged and x-ray therapy given. Again there was partial return of function. When last seen in November 1949, however, the patient once more complained of weakness of all the extremities and pain in the arms. Roentgenograms showed a decided advance in the destructive process.

Discussion. In this group there were 2 females and 1 male. The vertebrae from the 4th to the 7th cervical were involved, which is unusual according to some authors who believe that the tumor is more common in the upper cervical vertebrae. In all cases the lesion was extensive and preoperatively a diagnosis of metastatic malignant disease was made.

Lumbosacral Region. The 3 chordomas in this group occurred in 2 females and 1 male.

Case 11. A man, aged 60 years, in September 1943 "sprained" his back while lifting. He was hospitalized elsewhere for 3 weeks because of back pain. Roentgenograms taken at that time were reported as negative. He was well until January 1945, when he "felt something snap" in his lower back. Immediately thereafter he had severe pain in the back and difficulty in walking. Numbness and tingling of the legs and difficulty in starting urination were noted. In August 1945, a spinal cord tumor was suspected. Operation was undertaken elsewhere but no tumor was found. Roentgen therapy was given but the amount is not known. Following operation his legs became weaker. There was loss of both urinary and rectal sphincters. He complained of pain in the back and left flank which was aggravated by coughing, sneezing and lying down. He was admitted to the clinic in October 1946.

FIG. 19. *Case 11.* Roentgenogram, lateral view, showing narrowing of the 1st lumbar vertebra with osteoblastic and osteolytic changes.

Examination. There was marked weakness with muscle atrophy of the lower extremities. Superficial and deep reflexes were absent. Saddle anesthesia was present. Straight-leg-raising test was negative.

Roentgenograms of the spine showed marked osteoblastic and osteolytic changes of the 1st lumbar vertebra (Fig. 19). The destructive process involved the lower portion of the 12th thoracic and upper portion of the 2nd lumbar vertebrae as well and suggested a metastatic malignancy. Lumbar puncture yielded xanthochromic fluid containing 2925 mg./100 cc. of protein. Myelograms indicated a block at the 1st lumbar vertebra.

Operation (by K.E.L.). Laminectomy was done and a large extradural tumor was found about the cord, extending from the 11th thoracic to the 1st lumbar vertebra. The transverse process of the 1st lumbar vertebra on the left was replaced by neoplastic tissue. The tumor also extended out along the nerve roots. The vertebral bodies of the 11th and 12th thoracic and 1st lumbar were infiltrated. The bulk of the growth was removed. There was no intradural extension.

Microscopic Study. The tumor was a typical chordoma (Fig. 20).

Postoperative course was very unsatisfactory. The tissues healed poorly because

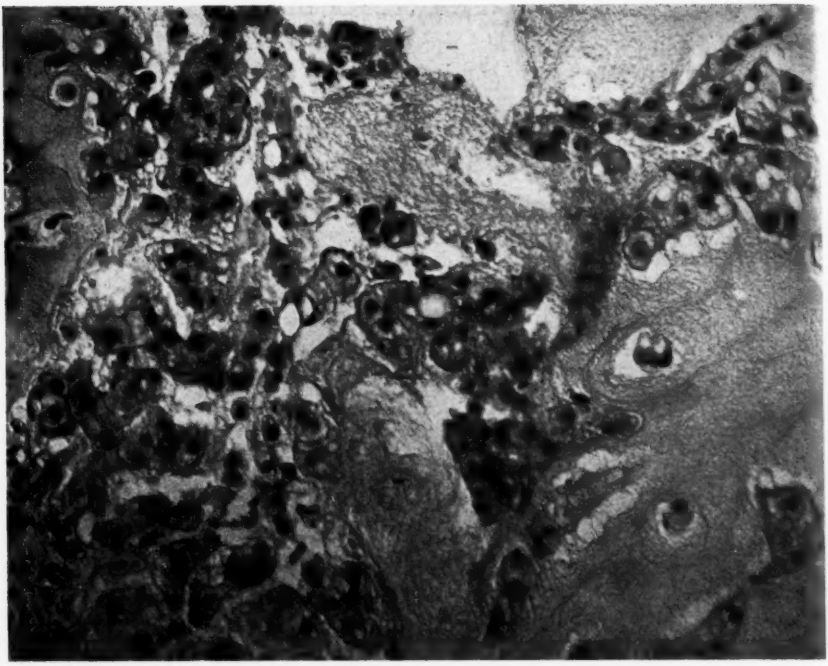


FIG. 20. *Case 11.* Photomicrograph of tumor.

of the previous roentgen therapy. Pain was very troublesome. Additional roentgen therapy was instituted but the patient failed steadily and died at home in May 1947.

Case 12. A woman, aged 36 years, was first seen in September 1942. She related that in 1935 lower sacral pain had developed. This was diagnosed as coccygodynia and part of the coccyx was removed. Some time later she began to have pain in the right leg, followed by loss of sensation in the rectum, vulva and buttocks, finally extending to the left leg. During 1939, bladder and rectal sphincteric control was lost. Since then there had been progressive "stiffness" of the legs and difficulty in walking. She had lost weight gradually, from 116 to 99 lbs.

Examination. There was obvious loss in weight. The patient walked with a shuffling gait. Both legs were weak, the left more than the right. Tendon reflexes at both the knees and ankles were hypoactive. There was complete anesthesia over the "saddle area" and down the posterior aspects of both legs from the 4th lumbar to the 2nd sacral segment.

Roentgenograms of the spine revealed extensive destruction of the laminae and bodies of the vertebrae from the 2nd lumbar to the 4th sacral. Osteoblastic activity, as well as a destructive process, was noted. Scalloping of the posterior bodies of the vertebrae typical of a chordoma was found.

Course. Roentgen therapy resulted in relief of pain but no change in the neurologic status.

Operation (by J.L.P.). On March 5, 1943, exploration was done from the 2nd lumbar to the 4th sacral vertebra. The spinous processes and laminae of these verte

brae were eroded and paper-thin. A huge extradural tumor was found. It was white, smooth and appeared encapsulated. The dura and the bodies of the sacral vertebrae were eroded. As much of the tumor as possible was removed without injury to the nerve roots.

Microscopic Diagnosis. The neoplasm was a typical chordoma.

Postoperative course was uneventful. Roentgen therapy was instituted as soon as the incision healed. The patient could soon walk better and some urinary sphincteric control developed.

From April 1943 to November 1946 there was steady improvement and the patient was able to return to her former occupation. When seen in November 1947, she was dragging the right leg and complained of pain in the lower back and right leg. Further roentgen treatment was given. This was followed by improvement until April 1949, when weakness and pain in the right leg recurred. A third series of roentgen treatment was given. In November 1949 she returned for further study. She could get about only on crutches, had involuntary spasmodic movements of the legs and was often incontinent. At that time the right knee and ankle jerks were almost absent. There was definite saddle anesthesia. Roentgenograms showed destruction of the 4th and 5th lumbar vertebrae. A large tumor mass could be seen in the psoas region. More spicule formation was noted about the tumor. Additional roentgen therapy has given relief of pain up to the present time.

Case 13. A woman, aged 18 years, was first seen in November 1946, when she complained of pain in the left leg of 3 years' duration which was gradually progressive. For 4 months there had been "numbness" in the leg, together with sensations of "stiffness" and "soreness." Recently, she had noted some difficulty with voluntary motion. There was no complaint of sphincteric control.

Examination. The patient was very uncomfortable when lying down. Acute tenderness was found on percussion of the sacrum and the 4th and 5th lumbar spinous processes. There was a lumbar lordosis with a list to the right. Straight-leg-raising test was positive bilaterally at 30°. Both knee and ankle jerks were considerably diminished. Hypesthesia to pain and touch was present over the 4th and 5th lumbar dermatomes, but not in the saddle area.

FIG. 21. *Case 13.* Roentgenogram demonstrating appearance of bone destruction.

Roentgenograms of the spine showed diffuse bony destruction starting at the 1st sacral vertebra and involving almost the entire sacrum (Fig. 21). The 1st sacral vertebra had slipped forward from the 2nd sacral as a result of the marked erosion. Some new bone formation was present in the alae of the 1st and 2nd sacral vertebrae.

Lumbar puncture yielded clear colorless fluid with a total protein of 34 mg. A pantopaque myelogram demonstrated complete block at the 4th lumbar segment.

Operation (by J.L.P.). A large, reddish, friable extradural tumor, which bled profusely, was found arising from the posterior aspects of the upper sacral vertebrae. The bone was eroded and the tumor was curetted out. No intradural extension was detected.

Microscopic Study. The tumor was composed of densely packed masses of both large and small cells (Fig. 22). It was thought that it was a fast-growing chordoma.

Postoperative course was uneventful. When the incision was healed roentgen therapy was started, with relief of pain and improvement in walking.

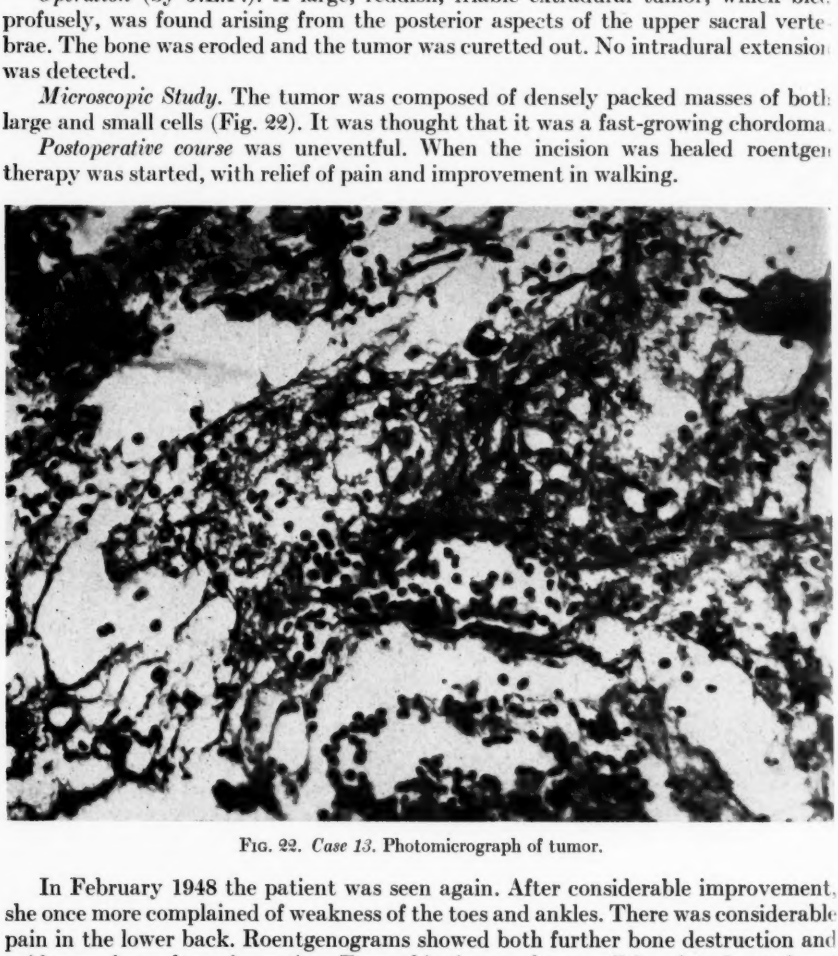


FIG. 22. *Case 13.* Photomicrograph of tumor.

In February 1948 the patient was seen again. After considerable improvement, she once more complained of weakness of the toes and ankles. There was considerable pain in the lower back. Roentgenograms showed both further bone destruction and evidence of new bone formation. From this time on her condition deteriorated and she died on May 31, 1948.

Discussion. Chordomas of the vertebral column appear to occur a little more frequently than the intracranial type. Many excellent reviews have appeared, especially those of Faust *et al.*,[3] Adson *et al.*,[1] Fletcher *et al.*,[2] and Morris and Rabinovitch.[9]

In our experience, the tumors have all been extensive. The spinal cord, cauda equina and roots have been compressed most often by an extradural

mass, but at times the dura has been penetrated and intradural extension has been marked.

Bony involvement occurred early in the course of the disease, and it seems likely that the tumors spread widely in the vertebral bodies and laminae before they encroach upon the cord. Certainly the tumor displays an embryonal facility for easy penetration in its invasion of bone, dura and nervous tissue. We did not encounter any encapsulated tumors that could be shelled out as described by Adson *et al.*[1]

Neither clinical history nor examination revealed anything that we thought was characteristic of a chordoma. The roentgenologic examination was most helpful in revealing the position and extent of the lesion but was of little help in determining the etiology. The bony involvement, of which destruction was the biggest element, nearly always suggested metastatic carcinoma. In several instances sclerosis and new bone formation were noted. This point does not seem to have been stressed in the past, and because of this our radiologists have opposed the diagnosis. Others, as well as ourselves, however, have frequently seen new bone and cartilage formation on microscopic examination of chordomas, so it does not seem untoward that these same findings should be seen radiographically; however, we have seen this only in the cases of chordomas of spinal origin.

COMMENT

Wherever chordomas are situated they look more or less alike. They appear as lobulated, gelatinous masses, often with a thin type of capsule. When incised, the tissue is soft, yellowish or raspberry jelly-like and can sometimes be aspirated with a large suction tube. Occasionally a chordoma may be a firm, red, cartilaginous mass.

Penetration of the dura may lead to the correct diagnosis. This is an uncommon occurrence with any type of tumor except chordomas (including the benign sessile tumors on the clivus). In all but one of our cases the tumors penetrated the adjacent bone, without any definite boundary. Only in Case 4 was it possible to separate the tumor clearly from the occipital bone. Veins and lymphatics are entered with ease.

It has now been established that a few chordomas metastasize. They certainly show great histologic variation, as can be seen in the photomicrographs. Considerable variation is found within a single tumor. If one uses the general pathologic criteria for degree of malignancy, as density of cells, mitoses, lack of intercellular material and variation of cellular and nuclear sizes, the rapidity of growth can be estimated with some degree of accuracy. As Godtfredsen pointed out, most often the clinical progression and histologic picture do not seem to agree. This was true in our cases. Although it has been repeatedly stated that most patients do not live much longer than 8 months after they are seen, and this was generally true of our series, none the less symptoms are often present for years before the patient seeks treatment. Also, since the nervous system is impaired by compression, it is

almost impossible to determine how long a chordoma may have been growing in bone before it emerges and produces symptoms. Some patients have been known to live a decade, and 2 of our patients have lived more than 6 years since the tumor was verified.

We are in agreement with the statements that rarely can the tumor be completely removed by surgery. This appears to have been possible in only one of our intracranial cases (Case 6) and in none of the spinal cases. Nor are we prepared to say what value roentgen therapy may have. It was not used in any of our cases of intracranial tumors, although Cases 1 and 7 had been given dosages considered adequate for a pituitary adenoma, without appreciable effect.

A somewhat different procedure was used with the tumors arising in the spine. These patients all survived the immediate postoperative period and could be treated over a period of time. Case 9 received no roentgen treatment either preoperatively or postoperatively and was alive 8 years later without signs of recurrence. Patients are known to be alive 15 to 18 years after the diagnosis of a chordoma has been verified, so that the survival period after roentgen therapy must be scrutinized carefully. Case 10 had received a maximal skin dose before operation, but the tumor growth was steadily progressive and he died 4 years after the onset of symptoms. Large doses were used in Case 8, with only transient effects, and a smaller dose used in Case 12 was ineffective.

Case 7 is alive and much improved 2 years after operation and roentgen therapy, but this is too short a period to be significant. Only in Case 8 does there appear to have been definite improvement following roentgen therapy. Soft tissue masses have receded and neurologic symptoms have subsided. Bony destruction proceeds slowly, however, and the patient seems to have been losing ground slowly.

It would appear that despite the fact that chordomas are embryonal tumors, they are highly resistant to x-rays. We believe roentgen therapy should be used, but the doses must be very large to be of value. The new supervoltage rays may be more beneficial.

Differential diagnosis may be difficult. As noted previously, the roentgenologic appearance is not characteristic, and most often a diagnosis of metastatic malignancy is made. For this reason we always prefer to perform a biopsy at least and, if possible, decompress the cord. Even the pathologist may have considerable trouble in making a final classification. Although many chordomas may be "typical," many are not, and have been confused with colloid carcinomas, sarcomas, myxochondromas and so forth.[2] This is especially true when diagnoses are made from quick frozen sections.

Givner[6] mentioned that roentgenograms not infrequently show calcified flecks in the tumor. We have not noticed this, but they have been seen histologically in some of our cases. At least 2 of our cases in which the tumor was of spinal origin showed bone formation following roentgen treatment, which was thought to be due to healing. We did not believe that this new

bone was neoplastic in origin, nor that its presence denied the possibility of the neoplasm being a chordoma, as some roentgenologists infer.

SUMMARY

The histories of 7 patients with intracranial and 6 with vertebral chordomas have been reviewed. Our experience in the diagnosis and treatment has been discussed. It is our belief that although a chordoma may often be suspected, there are no characteristic diagnostic signs. Although surgical treatment leaves much to be desired, an occasional patient may be benefited greatly, so that surgery should not be withheld. Roentgen therapy is mentioned but its value is still undetermined.

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NONOBSTRUCTIVE HYDROCEPHALUS

TREATMENT BY ENDOSCOPIC CAUTERIZATION OF THE CHOROID PLEXUS

LONG TERM RESULTS

JOHN E. SCARFF, M.D.

Department of Neurological Surgery, College of Physicians and Surgeons, Columbia University, and the Service of Neurological Surgery, Neurological Institute of New York, Columbia-Presbyterian Medical Center, New York

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A SOUND rationale for the treatment of nonobstructive hydrocephalus was first proposed in 1918 by Dandy.[1] Having previously demonstrated that the choroid plexuses within the lateral ventricles were the principal source of the cerebrospinal fluid, he proposed the surgical extirpation of these plexuses as a means of reducing the quantity of fluid produced. He hoped in this way to establish a balance between the rate of secretion and the rate of absorption and thus reduce the abnormal intraventricular tension occurring in nonobstructive hydrocephalus.

Dandy described an operation which consisted first of complete drainage of the lateral ventricles, followed by surgical excision of the plexuses. Unfortunately, complete drainage of the ventricles was accompanied by collapse of their thinned-out walls, resulting in severe shock and a high operative mortality. This is graphically described in Dandy's own words:

> . . . death will follow almost immediately on the release of the fluid. . . . In the advanced cases we can hold out very little encouragement from operative procedures of any kind which will necessitate the release of fluid and collapse of the brain. In 3 (out of 4) cases of this series . . . there was an immediate operative collapse beginning with pallor of the face and body, rapid feeble pulse which quickly became imperceptible, cold clammy perspiration, rapid shallow and irregular respiration. . . . These things invariably began with evacuation of ventricular fluid. . . . Following escape of the fluid, the thin brain walls collapse. . . . The mechanical kinking of the larger vascular trunks by angulation of the infolding brain must have a pronounced effect on circulation.

Although Dandy reported in his original article having operated on 4 patients by this method, only 1 survived. No subsequent cases so treated were ever reported by him.

Endoscopic cauterization of the choroid plexuses was tentatively tried but rejected by Dandy in 1922. However, the value of this technique was clearly demonstrated by Putnam in 1934,[2] and a few months later by the present writer[4] (Fig. 1). The ventriculoscopes developed by these two workers differed considerably in their construction, but the surgical principle behind their use was the same, namely, destruction of the choroid plexuses without removing the cerebrospinal fluid from the ventricles. This prevented

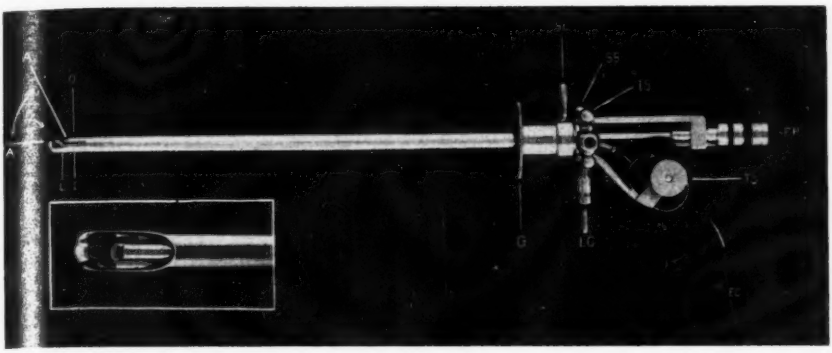


FIG. 1. The author's ventriculoscope. The fore-oblique lens system provides a field of vision corresponding to one-half of a flat cone. The visual angle is roughly indicated by lines A-A_1. A unipolar cautery (C) can be advanced or retracted as desired by means of the thumb screw (TS). Irrigating fluid for the operative field is brought into the instrument by way of stop cock connections (IS), whence it is conducted through narrow tubes to the operating tip of the instrument (I). A small light bulb is situated at each side of the lens aperture in the operating end of the instrument. LC is the lighting connection leading to a battery box. EC is the connection between the movable cautery and the electrosurgical unit. (Photograph reproduced by courtesy of American Cystoscope Makers, Inc.)

collapse of the thinned-out cortex and enormously decreased operative shock and consequent mortality (Fig. 2).

The technique employed by the writer for performing endoscopic cauterization of the choroid plexuses is here described.

TECHNIQUE

As a rule, Avertin is used as an anesthetic. The infant is operated upon in the prone position with the face resting in a simple canvas hammock. Two small incisions are made over the parietal bossae; these incisions are slightly larger than those used for ventriculography, and somewhat more anterior and lateral in location. It is desirable to get them as far forward as can be safely done without injuring the pre- or postcentral gyri. Immediately after the scalp incisions have been made, galeal sutures are placed in anticipation of the closure; these are set close enough together to make subsequent closure of the galeal layer water-tight. An opening in the bone, approximately 2 cm. in diameter, is then made on each side. The dura is opened through a cruciate

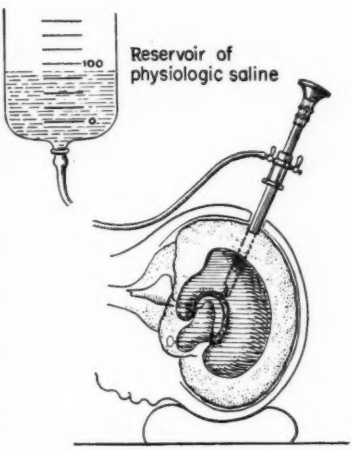


FIG. 2. Technique of endoscopic cauterization of the choroid plexuses. Note the direct communication between the ventricles and a reservoir of Ringer's solution, by means of which constant pressure is maintained within the ventricles throughout the operation. This prevents collapse of the thinned-out cortex and minimizes operative shock.

incision, which is just large enough to admit the sheath of the ventriculoscope. A small opening through the cortex into the ventricle is then made with a blunt instrument, and the shaft of the ventriculoscope is introduced into the ventricle.

From this point on, the operation is carried out by vision through the lens system of the endoscope. When thus seen, the choroid plexus looks like a fungus, light pink in color, on the floor of the ventricle. The tip of the electrode is then passed lightly over the surface of the plexus, which is immediately coagulated and becomes chalky white. The plexus can usually be coagulated from the foramen of Monro, backward past the glomus, and well into the temporal horn. When this is completed, the instrument is withdrawn, and the ends of the galeal sutures are quickly tightened and tied. Following this, a row of interrupted cutaneous sutures completes the closure.

The cauterization itself requires approximately 10 to 15 minutes, during which short time the intraventricular fluid pressure is maintained constantly at a normal level by means of an irrigating system within the ventriculoscope. The writer regularly employs standard Ringer's solution in this irrigating system.

The cauterization is then carried out in similar fashion on the opposite side at the same session.

The author's experience indicates that the most radical cauterization which can be achieved at a single session is the best. Occasionally there is a postoperative hypotension within the ventricles and cranium, evidenced by progressive retraction of the fontanelle and accompanied by progressing irritability and elevation of pulse and respiratory rates. When such ventricular hypotension occurs, it can be easily dealt with by tapping one of the ventricles through the anterior fontanelle and allowing Ringer's solution to enter the ventricle under gravity pressure until the fontanelle is again flush with the cranium. It has never been necessary to do this in any one case more than two or three times, and only during the first or second postoperative day. Thereafter, some natural balance between production and absorption of cerebrospinal fluid is reached.

In 1943, Putnam[3] reported 42 children operated upon between 1934 and 1942 inclusive. There were 11 "hospital deaths" (25 per cent), 15 "later deaths" (33 per cent), and 16 "survivors" (42 per cent). Of these 16 operative survivors, 1 was reported in good physical and mental health 9 years after operation, 2 at 6 years after operation and 1 at $3\frac{1}{2}$ years after operation.

The present paper reports the results obtained with endoscopic cauterization of the choroid plexus in the treatment of infants suffering from nonobstructive hydrocephalus. These cases are reported in two series.

The first series consists of 20 infants operated upon before the war, beginning with the first case in 1935 and including without omission all cases until the end of 1941. The results in this series are as follows: number of cases—20; hospital deaths—3 (15 per cent); survivals without permanent relief of intracranial pressure—7 (35 per cent); survivals with permanent relief of pressure—10 (50 per cent).

Of the 10 children in this first series who realized permanent relief of pressure, one died 5 years after operation of undetermined cause, a second died 9 years after operation of undetermined cause, and a third died 10 years after operation of pyogenic meningitis. A fourth child died 13 years after

operation following ill-advised ventriculography carried out as part of a routine follow-up study.

Six children are now living. Three of these, now 14, 12, and 11 years old respectively, are physically well but mentally retarded. Three children, 13, 12 and 11 years old, are in their appropriate grades in school and receiving average or better than average marks. A detailed summary of the 20 cases in this first series is given in Table 1.

The second series consists of 19 infants operated upon since 1946. The results in this series are as follows: number of cases—19; hospital deaths—1 (5 per cent); survivals without permanent relief of intracranial pressure—3 (15 per cent); survivals with permanent relief of pressure—15 (80 per cent).

The follow-up periods for this second series are not yet long enough to determine the children's intellectual ceilings, but results thus far indicate that 11 of them, representing 58 per cent of the series, have average mentality for their ages. A detailed summary of the 19 cases in this second series is given in Table 2.

TABLE 1

Results obtained in the treatment of nonobstructive hydrocephalus by endoscopic cauterization of the choroid plexuses

FIRST SERIES, as reported in 1942,[5] with *follow-up reports* to August 1, 1951

Case, Age, Date of Op.		Postoperative Result
		Group 1. Hospital deaths
1. A.R. 1935	7 mos.	Immediate postop. status good, but slight twitchings of extremities began 7 hrs. after op. 12 hrs. after op., onset of tonic and clonic convulsions, hyperthermia. Died.
2. J.W. 1937	6 wks.	Immediate postop. status good, but intermittent spastic states began 3 hrs. after op. 6 hrs. after op. sudden opisthotonos and respiratory failure. Died.
3. F.F. 1935	4 mos.	Immediate postop. status good, but cardiac decompensation and pulmonary edema appeared due to too large and too rapid blood transfusion. Died, but not an op. death.
		Group 2. Survivals without permanent relief of pressure
4. J.B. 1938	8 mos.	Op. technically unsatisfactory. Lived 3 mos. after op. Died at home; details of death not known.
5. C.O. 1938	5 mos.	Pressure relieved temporarily. 1 yr. after op. still alive, mentally dull, fontanelle full and head slowly enlarging.
6. L.P. 1940	3 mos.	Pressure relieved temporarily, but recurred. Re-op. 1 mo. later did not relieve pressure. 1 yr. after op. still alive, mentally bright, but fontanelle full and head slowly enlarging.
7. R.M. 1937	4 yrs.	Pressure relieved at time of hospital discharge, but death at home 4 mos. after op. following unexplained acute febrile illness. Decompression areas soft at time of death.
8. J.C. 1937	7 wks.	Temporary improvement. At time of discharge fontanelle depressed and smaller, head smaller. Died of acute bronchopneumonia 1 yr. after op.
9. I.M. 1937	12 wks.	Condition good at time of hospital discharge, but died 4 mos. later at home; no details of death available.
10. H.F. 1940	7 mos.	Fontanelle soft and depressed after op., but progressing downhill course marked by opisthotonos. Died 20 days after op.

Case, Age, Date of Op.	Postoperative Result
	Group 3. Survivals with permanent relief of pressure
11. A.O'C. 1 mo. 1934	Preop., very advanced hydrocephalus, with head 25 in. (64 cm.) in circumference. Patient survived, learned to walk and talk, but was mentally defective. In 1939, 5 yrs. after op., died of causes unrelated to hydrocephalus.
12. A.V. 5½ mos. 1935	Preop., advanced hydrocephalus, with head 21 in. (53 cm.) in circumference. Intracranial pressure relieved by op. Child lived for 9 yrs., but was mentally defective. Died in 1944 of causes unrelated to hydrocephalus.
13. K.G. 5 mos. 1936	Preop. advanced hydrocephalus, with marked enlargement and distortion of head. Intracranial pressure permanently relieved by op. Child was moderately retarded mentally. In 1946, 10 yrs. after op., he had an acute febrile illness (T. 106°), clinically diagnosed meningo-encephalitis. He ran a high febrile course and died after 40 days. Autopsy revealed basilar meningitis from which hemolytic staphylococcus aureus was recovered.
14. E.H. 2 mos. 1936	Preop. advanced hydrocephalus and large lumbar meningocele. Following removal of meningocele and cauterization of choroid plexus, she lived for 14 yrs. without signs of intracranial pressure. However, she was mentally defective. During this time there was precocious development of secondary sexual characteristics. In 1949, she was recalled to hospital for follow-up studies. 5 hrs. after ventriculography, she suddenly died. No autopsy; cause of death was never determined.
	The following 6 patients are still living:
15. R.C. 3 mos. 1937 581140	Preop. advanced hydrocephalus. Thickness of cortex at time of op.: right 0.5 cm., left 1.5 cm. Intracranial pressure permanently relieved by cauterization of choroid plexus. Patient is still living 14 yrs. after op. He is well developed without gross physical deformity; ambulatory without gross motor deficiency but with slight incoordination in movements of all extremities. Vision is apparently normal. He exhibits precocious development of external genitalia. He is neat in appearance, quiet and cooperative but shows very little spontaneous activity. Answers are monosyllabic. Psychometric tests: 2-yr. intellectual level. (*Figs. 3 and 4*).
16. M.A.T. 4 mos. 1938 591017	Preop. advanced hydrocephalus. At op. cortex was 1 cm. thick. Permanent relief of abnormal intracranial tension. 13 yrs. after op. patient is still alive. There is slight spastic weakness of right lower extremity and poor coordination in movements of all extremities. Vision apparently is normal. She is neat in appearance, pleasant in manner, well behaved and cooperative. She has passed 6th grade English, spelling and reading, but has not been able to get beyond 3rd grade arithmetic. She reads much on her own initiative. Psychometric tests: "low average intelligence." (*Figs. 5 and 6*).
17. A.J. 3 mos. 1939 569471	Preop. well advanced hydrocephalus. Frontal cortex 1.8 cm. in thickness; parietal, 1 cm.; occipital, 0.3 cm. Abnormal intracranial pressure permanently relieved by cauterization. Today, 12 yrs. after op. patient is living and well. She is vivacious, attractive and charming, has easy poise and nice manners. There is slight incoordination in all fine movements. However, she participates actively in dancing, swimming and gymnastics, and plays the piano quite well. In an excellent girls' school she was abreast of her own age group, with an overall average of B. The headmistress wrote in 1949, 10 yrs. after op.: "A— has shown excellent progress during her recent school year. You will see that I have added to her school record the result of her last intelligence test. An I.Q. of 124 shows excellent ability, and I hope as time goes on A— will be prepared for college. This I.Q. shows that she is well able to do advanced academic work." This child's family moved to another country in 1949, but reports from her father indicate continuing normal development. (*Figs. 7 and 8.*)

Case, Age, Date of Op.	Postoperative Result
18. J.K. 2 yrs. 1939 585082	Patient had had normal birth and development until he was 2 yrs. old. Then he had meningococcus meningitis, treated with sulfanilamide. Acute nonobstructive hydrocephalus developed leading to coma. He was op. on as an emergency. At op. cortex was 2 cm. in thickness. Intracranial pressure was permanently relieved by bilateral cauterization of the choroid plexus. This is the first report of postmeningitic hydrocephalus successfully treated by cauterization of the choroid plexuses. 12 yrs. after op. patient is still living and well. Physical development has been good, and he is large for his age. He is very active and in many respects an attractive boy. However, he is a disciplinary problem; he obeys his father of whom he is afraid but will not obey his mother. He is mentally retarded with an I.Q. of 64. (*Figs. 9 and 10*).
19. F.R. 3 mos. 1940 614190	Preop. fairly early case of hydrocephalus, with head 41.5 cm. and greatly enlarged, bulging and tense anterior fontanelle. At op. cortex was 1.5 cm. in thickness. 11 yrs. after op. patient is living and well without symptoms or signs of recurrent intracranial pressure. He is attending public school, is 1 yr. ahead of his age group and maintains an average of B+ in his studies. (*Figs. 11 and 12.*)
20. M.S. 5 mos. 1940 793241	Preop. cortical thickness: frontal 1 cm.; right parietal 2 mm.; left parietal 1 cm.; right occipital 2 mm.; left occipital 1.5 cm. 11 yrs. after op. patient is living and well without symptoms or signs of recurrent pressure. She is a nice appearing Negro child, neat, shy and quiet. There has been precocious development of secondary sexual characteristics. At home she helps her mother and takes care of younger children. She is definitely defective mentally; I.Q. 58. (*Figs. 13 and 14.*)

Tabulation: Hospital deaths—3 (15 per cent).
Poor results, that is, discharged from hospital but without permanent relief of intracranial pressure—7 (35 per cent).
Good results, that is, discharged from hospital with permanent reduction of intracranial pressure to normal levels—10 (50 per cent).
Long-term survivals with average or better than average mentality—3 cases or 15 per cent of series.

TABLE 2

Results obtained in the treatment of nonobstructive hydrocephalus by endoscopic cauterization of the choroid plexuses

SECOND SERIES, 1946 through 1949. Reported as of August 1, 1951

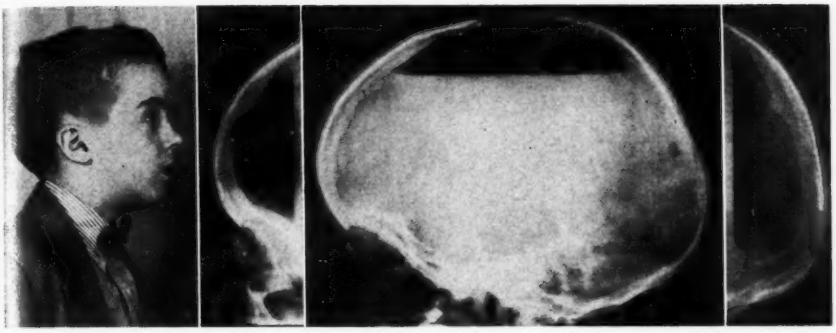
Case, Age, Date of Op.	Postoperative Result
1. C.G. 640801 7 mos. 4-18-41 (omitted from first series through oversight)	*Good.* Patient discharged 3 wks. after op. with pressure relieved. In 1949 she fell, sustaining a ruptured spleen, and died of pulmonary infarct following abdominal surgery. She had been in good health for 8 yrs. without increased intracranial pressure; somewhat retarded mentally.
2. J.L. 797141 8 wks. 1-5-46	*Good.* Patient discharged on 11th postop. day with pressure relieved. 5 yrs. later is alive, well, walking and talking. Greatly retarded mentally.
3. W.P. 831570 6 mos. 6-24-46	*Good.* Preop. purulent cerebral meningitis successfully treated with antibiotics. Nonobstructive hydrocephalus developed. 5 yrs. after cauterization, patient is physically active, without symptoms or signs of recurrent pressure, but mentally retarded.

Case, Age, Date of Op.	Postoperative Result
4. J.G. 832553 11 wks. 7-22-46	*Good.* Preop. pneumococcus meningitis, successfully treated with antibiotics. Nonobstructive hydrocephalus developed. Discharged from hospital 3 wks. after op. 5 yrs. later, patient is alive, physically well, without symptoms or signs of recurrent pressure, but mentally defective.
5. W.D. 828156 4 mos. 9-27-46	*Good.* Patient discharged 1 wk. after op. 5 yrs. later, is alive and well, without symptoms or signs of recurrent pressure. Apparently normal mentally. (*Fig. 15.*)
6. L.B. 821114 1 yr. 10-25-46	*Poor.* Incomplete reduction of intracranial pressure; died 5 mos. later from hydrocephalus.
7. R.L. 845707 1 mo. 11-29-46	*Poor.* Immediate relief of pressure signs lasting 3 mos. after op.; then pressure recurred. Generalized convulsions; head enlarged.
8. H.H. 855738 1 yr. 1-29-47	*Good.* Patient discharged on 9th postop. day with pressure relieved. 4½ yrs. later, he is alive and well, without symptoms or signs of recurrent pressure. Apparently normal mentally. (*Fig. 16.*)
9. E.M. 856398 8 mos. 3-8-47	*Good.* Patient discharged on 15th postop. day with pressure relieved. 2 yrs. later, no recurrence of pressure; child beginning to walk and talk.
10. S.G. 863918 1 yr. 3-31-47	*Poor.* Pressure unrelieved. Op. repeated 18 mos. later. Pressure persisted. 2½ yrs. after first op. family physician wrote that head was still enlarging and bone flap bulging.
11. S.M. 855014 6 mos. 4-1-47	*Good.* Hydrocephalus secondary to toxoplasmosis. Cauterization followed by relief of pressure for 2 yrs. Progressive mental deterioration and convulsions, ? due to toxoplasmosis. No recurrence of intracranial pressure.
12. R.D. 864096 8 mos. 4-19-47	*Good.* Patient discharged 2 wks. after op. with pressure relieved. 4 yrs. after op. pressure apparently still normal, but child is mentally defective with some motor disability.
13. J.V. 867800 9 mos. 5-6-47	*Died.* Patient expired on 5th postop. day following convulsions. Autopsy showed destructive lesions in thalamus.
14. J.R. 835961 4 yrs. 5-8-47	*Good.* Patient discharged on 17th postop. day with pressure relieved. 4 yrs. after op. there is still no sign of recurrent pressure. Child seems normally intelligent. (*Fig. 17.*)
15. B.B. 858186 5 mos. 5-17-47	*Good.* Pressure relieved by op. 4 yrs. later child is alive and well, without symptoms or signs of recurrent pressure. (*Fig. 18.*)
16. T.C. 851356 4 mos. 6-18-47	*Good.* Preop. encephalomeningocele. Pressure relieved by cauterization. Patient discharged on 20th postop. day. 4 yrs. later is alive and well, without signs of recurrent pressure. (*Fig. 19.*)
17. E.W. 876255 4 mos. 7-22-47	*Good.* Pressure relieved by op. 4 yrs. later patient is walking and talking, in excellent health and apparently normal mentally. (*Fig. 20.*)
18. J.K. 894107 3 yrs.	*Good.* Pressure relieved by op. 3½ yrs. later patient is walking and talking normally. She appears unusually bright for her age. (*Fig. 21.*)
19. J.B. 867789 3 yrs. 1-23-48	*Good.* Patient discharged on 10th postop. day with pressure relieved. 3½ yrs. later he is in excellent condition physically and mentally. (*Fig. 22.*)

Tabulation: Hospital deaths—1 (5 per cent).
Poor results—3 (15 per cent).
Good results—15 (80 per cent).
Survivals with average or better than average mentality—11 (58 per cent).

DISCUSSION

In the author's second series of cases operated upon since 1946, there was only a 5 per cent operative mortality, whereas 80 per cent of the children operated upon experienced permanent relief of intracranial pressure. These



FIGS. 3 and 4. R.C., First Series, Table 1, Case 15. (*Left*) The author's oldest surviving patient. He is now 14 years of age. He is a severe mental defective. (*Right*) Ventriculograms at time of operation.

FIG. 5. M.A.T., First Series, Table 1, Case 16. This child is now 13 years of age and is attending school. She has passed 6th grade English, spelling and reading but was unable to get beyond 3rd grade in arithmetic. Psychometric tests rate her as of low average intelligence (see Fig. 6).

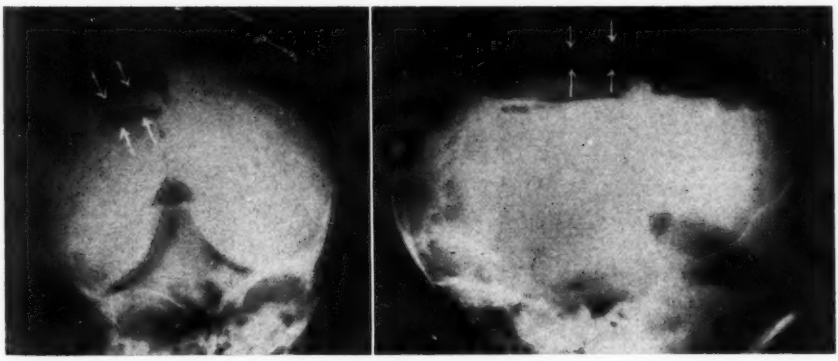
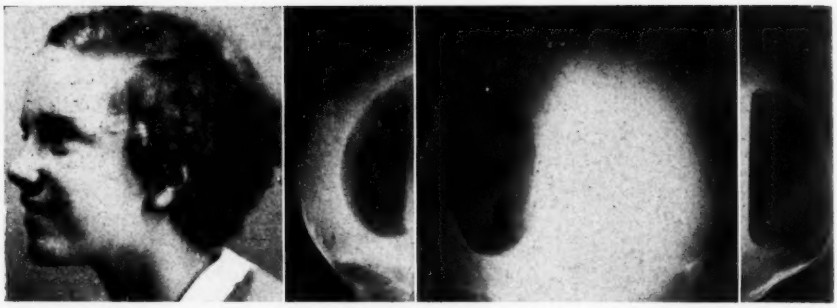


FIG. 6. M.A.T., First Series, Table 1, Case 16. Preoperative pneumoencephalograms. These are poor because of the small amount of gas and unequal replacement of fluid, causing collapse of the thin ventricular wall. However, they do show the thickness of the cortex, which measures about 1.5 cm.

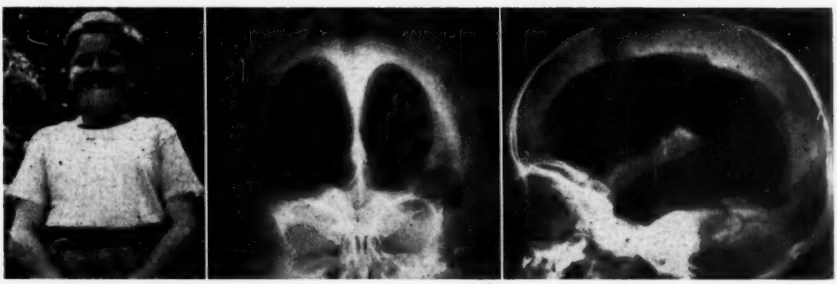


FIGS. 7 and 8. A.J., First Series, Table 1, Case 17. (*Left*) This child is now 12 years of age. She is keeping abreast of her class in school, with an I.Q. of 124. She also swims, dances, and plays the piano. (*Right*) Ventriculograms at time of operation.

figures clearly indicate that the technical problems of treating nonobstructive hydrocephalus have, on the whole, been mastered.

Interest today centers on the ultimate intellectual development that can be expected in children experiencing permanent relief of intracranial pressure as the result of operation. This poses two problems. The first is the necessity of recognizing early that hydrocephalus is present, and the second is the selection for surgery of only those children offering reasonable prospects of normal intellectual growth.

In respect to early diagnosis, it should be pointed out that all too often sole reliance is placed on the size of the infant's head. Tables indicating the standard rate of growth for infants' heads are given in all pediatric texts, but the cranial measurements are of relatively little value for establishing the presence of increased intracranial pressure in any individual case. The size of the head normally varies considerably among healthy infants. The relative circumference of head and chest is likewise valueless in many instances for

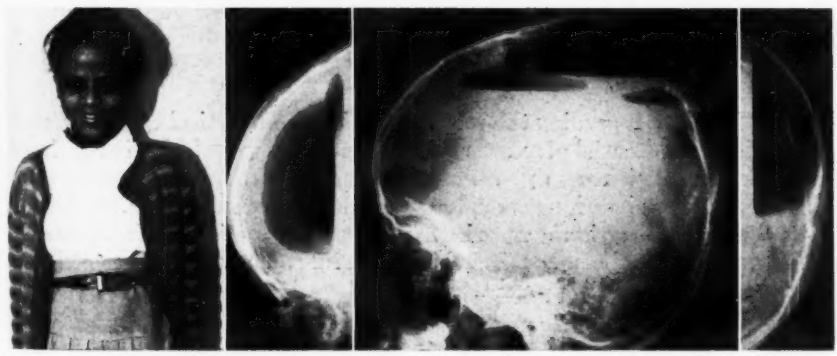


FIGS. 9 and 10. J.K., First Series, Table 1, Case 18. (*Left*) At the age of 2 years, hydrocephalus developed in this boy following the successful treatment of a meningococcus meningitis. He is the first reported case of postmeningitis hydrocephalus successfully treated by cauterization of the choroid plexus. The patient is now 12 years of age. He is an attractive boy to meet, but is a behavior problem. His I.Q. is 64. (*Right*) Ventriculograms at time of operation.

FIGS. 11 and 12. F.R., First Series, Table 1, Case 19. (*Left*) This 11-year-old boy is one year ahead of his age group in school and is averaging B+ in his marks. (*Right*) Patient at time of discharge from hospital following cauterization of choroid plexus in 1940. Preoperative ventriculograms have been lost, but photograph indicates the enlargement of head and anterior fontanelle.

the same reason. In the borderline case, even the rate at which the head grows provides no reliable information as to the presence of increased intracranial pressure.

The most reliable information regarding the state of intracranial pressure in infants is to be obtained from the anterior fontanelle. In the normal healthy child, the fontanelle is slightly depressed and pulsates when the child is held in the sitting position and is not straining or crying. If the fontanelle bulges under these conditions, abnormal intracranial pressure must be suspected. If, in addition, palpation reveals the fontanelle to be firm or tense, increased intracranial pressure is certain. When such a condition is found, the child should be admitted to the hospital for complete studies, including dye test and fractional ventriculography. These tests will reveal whether hydroceph-



FIGS. 13 and 14. M.S., First Series, Table 1, Case 20. (*Left*) This little colored girl is now 11 years old. She is neat, pleasant, and helpful to her mother. She was never able, however, to pass the first grade of school. Her I.Q. is 58. (*Right*) Ventriculograms at time of operation. In view of the air studies, it is interesting to note that this child shows no motor weakness, incoordination, or visual impairment.

alus is present, whether it is obstructive or nonobstructive, and finally and of great importance, the thickness of the remaining cerebral cortex.

It must be reiterated that the selection of cases suitable for surgical treatment cannot be based on the external size and shape of the infant's head. The only absolute indication or contraindication for definitive surgery is the thickness of the remaining cerebral cortex as revealed by ventriculography, since cortical thickness is the most important single determinant of the intellectual potential of the infant.

FIGS. 15–22. Second Series, Table 2. (Fig. 15) W.D., Case 5. (Fig. 16) H.H., Case 8. (Fig. 17) J.R., Case 14. (Fig. 18) B.B., Case 15. (Fig. 19) T.C., Case 16. (Fig. 20) E. W., Case 17. (Fig. 21) J.K., Case 18. Fig. (22) J.B., Case 19.

Very few data regarding the relationship between cortical thickness and the intellectual potential of hydrocephalic infants are to be found in the literature because, until recently, very few children operated upon for hydrocephalus have survived long enough to provide valid observations. However, on the basis of the writer's experience with the two series herein reported, he believes that a uniform cortical thickness of 2 cm. or more will permit an average intellectual development.

Two adults with congenital hydrocephalus arrested in childhood and many years later studied at the Neurological Institute lend support to this opinion. One of these, a girl 26 years of age, had completed high school, was regularly employed, and appeared to be normal in all respects. Following an acute infectious disease signs of increased intracranial pressure developed and she was admitted to the Neurological

Institute for diagnosis and treatment. A ventriculogram revealed a relative aqueduct insufficiency with marked hydrocephalus presumably of long standing; the cortex averaged approximately 2.5 cm. in thickness. Her I.Q. was 106, giving her an intellectual rating of average normal.

A second patient was a woman in her middle forties who for 20 years had been teaching school. Following an acute respiratory infection she too showed signs of increased intracranial pressure and was admitted to the hospital for diagnosis and treatment. The ventriculograms revealed atresia of the aqueduct of Sylvius with a marked hydrocephalus; the cortex measured approximately 2.5 cm. in thickness. The available evidence would indicate that the hydrocephalus was of many years standing, but the reduction in cortical substance had nevertheless allowed her to attain a useful and honored position in her community.

Cortical thickness of less than 1 cm. certainly precludes normal intellectual development, at least it has done so in these series of infants. The intellectual development that may be expected following successful reduction of intracranial pressure in those infants whose cortex is less than 2 cm. thick but more than 1 cm. has been unequal and unpredictable. This suggests the existence of factors other than cortical thickness alone as determinants of the child's ultimate intellectual attainment. For instance, one child (J.K., Series I, Case 18, Table 1) had a cortex of approximately 2 cm. and is rated as mentally deficient; whereas, another child (A.J., Series I, Case 17, Table 1) with cortex averaging no more and possibly slightly less in thickness has not only kept abreast of her age group in school but stands near the top of her class.

There is no way known at this time to ascertain preoperatively which of the infants with cortexes between 1 and 2 cm. thick will develop normally and which will not. Preoperative cytoarchitectural studies may some day provide such information. On the basis of present knowledge, however, the only conclusion possible is that the infant with a cortex between 1 and 2 cm. thick appears to have a 50 per cent chance of average mental development. For the time being, all the surgeon can do in such an instance is to present the facts to the parents and ask them to share in the decision as to whether operation should be performed on their child.

SUMMARY

1. The author reports the results obtained by him in the treatment of nonobstructive hydrocephalus by endoscopic cauterization of the choroid plexus in two series of infants.

2. In a series of 20 children operated upon prior to 1942, there were 3 hospital deaths, 7 survivals without permanent relief of intracranial pressure, and 10 survivals with permanent relief of pressure. Of these last 10 children, 6 are still living, and 3 of them have average mental development for their ages.

3. In a series of 19 children operated upon since 1946, there were 1 hospital death, 3 survivals without permanent relief of intracranial pressure, and

15 survivals with permanent relief of pressure. Eleven of these 15 children have average mental development.

4. The most reliable sign of early hydrocephalus in infants is to be found in the state of the anterior fontanelle.

5. The best criterion known at this writing for the selection or rejection of cases for surgery is to be found in the thickness of the remaining cerebral cortex as revealed by ventriculography.

6. The author believes that a uniform cortical thickness of 2 cm. will usually assure an average intellectual development, whereas a cortical thickness of less than 1 cm. will preclude it.

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VASCULAR LESIONS IN PITUITARY ADENOMAS*

C. F. LIST, M.D.†, J. R. WILLIAMS, M.D., AND G. W. BALYEAT, M.D.
Grand Rapids, Michigan

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THE textbook picture of a disease is developed by isolating schematically its salient features from a large variety of clinicopathologic observations and by attempting to reduce them to a common denominator. This endeavor of systematization certainly gratifies the urge of logical thinking, but by its arbitrary simplification tends to construct a fixed pattern which is only reluctantly discarded if new and perhaps contradictory facts are discovered.

A good example of such a situation is found in our state of knowledge concerning hypophyseal adenoma. The well-known textbook concept of this type of neoplasm dates back to Cushing's classical description. With growing experience, however, confusing and therefore neglected variants of the disease had to be reconsidered. Jefferson,[5] for instance, gave an excellent analysis of unusual pituitary adenomas with extrasellar extension.

In this article we propose to depict another aspect of the kaleidoscopic pituitary syndrome, viz., the vascular lesions occurring in pituitary adenoma. Knowledge of this condition is by no means new, and sporadic reports may be found even in the older literature. Brougham, Heusner, and Adams[1] deserve credit for having collected all these reports; and on the basis of 5 new observations have redirected our attention to the problem. Since their publication we were able to find 3 additional articles dealing with this subject.[4,6,7]

The paucity of references in the literature may have created the impression that vascular lesions in pituitary tumors are very rare; but the discussion following the delivery of our paper at the Harvey Cushing Society meeting in April 1951 convinced us that similar cases are not exceptional at all, and that they pose challenging diagnostic and therapeutic problems. Whereas Brougham, Heusner, and Adams' paper dealt with 5 clinicopathologic observations verified by autopsy, we wish to present in full 3 clinical cases with favorable outcome. The first case was seen by one of us at the University of Michigan Hospital.‡ The other two observations were made in private practice.

Case 1. University of Michigan Hospital No. 538669. G. T., female, aged 42. Admitted Dec. 16, 1943. Discharged Jan. 26, 1944.

History. The patient had been in good health except for amenorrhea which followed appendectomy 15 years ago. Two weeks prior to admission, she complained

* Presented at the meeting of the Harvey Cushing Society, Hollywood, Florida, April 27, 1951.

† 29 Sheldon Avenue, Grand Rapids 2, Michigan.

‡ We wish to express our appreciation to Dr. E. A. Kahn who kindly permitted us to publish this case.

of severe right supraorbital headache and difficulty in elevating the right upper eyelid. Within a few days, vision of the right eye gradually declined, finally progressing to total blindness. She became confused, restless, and, on the day before admission, lapsed into a semicomatose state.

Examination. The patient was semicomatose, disoriented, incoherent, and resistive. Temperature 105.6°; pulse 130; respirations 16. B.P. 90/70. Her skin was of unusually fine texture, white and dry. Pubic and axillary hair were absent. There

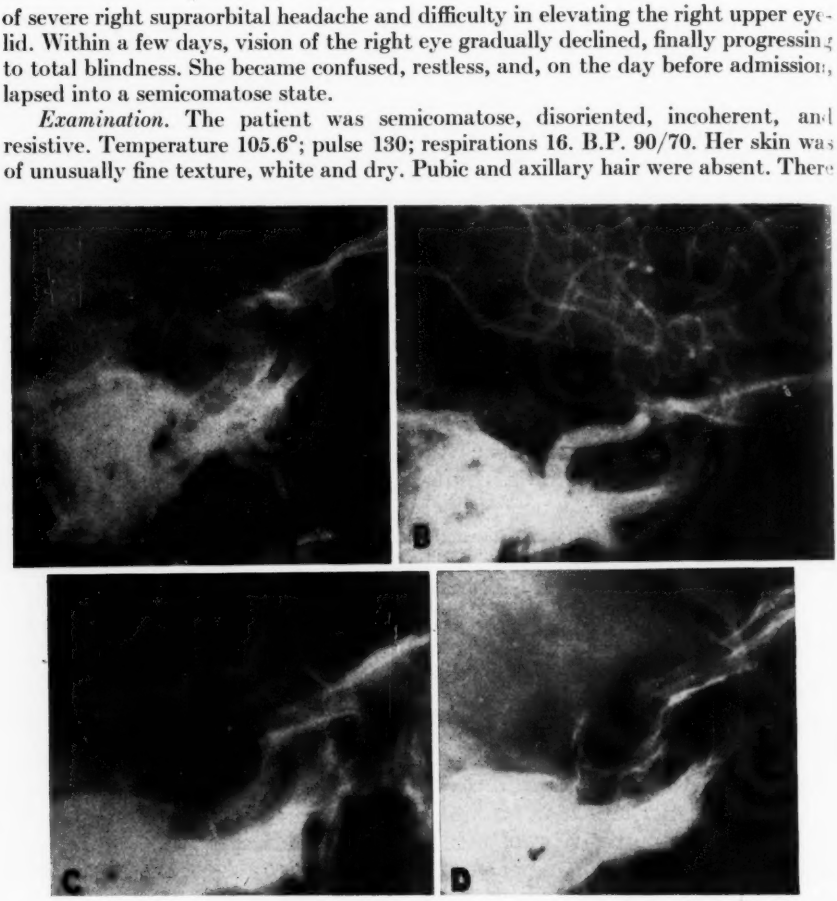

FIG. 1. (A) *Case 1.* Enlarged sella. (B) *Case 2.* Arteriogram. Note slightly erect and opened carotid siphon. (C) *Case 3.* Intrasellar erosion. (D) *Case 3.* Recalcification and reduction in size of the sella following x-ray therapy.

was marked nuchal rigidity and Kernig's sign was positive bilaterally. Both pupils were fixed to light, the right one being dilated. There was also a right-sided ptosis of the upper lid and divergent strabismus indicative of a 3rd nerve palsy. The patient did not respond to light stimuli. The fundi showed slight blurring of the nasal disk margins. She moved all her extremities spontaneously and equally. The plantar responses were extensor, and a right-sided Rossolimo sign was present. The abdominal reflexes were absent.

The clinical impression was that of spontaneous subarachnoid hemorrhage, probably from ruptured basal aneurysm on the right.

Lumbar puncture yielded a brick-red fluid under pressure of 280 mm. The fluid was loaded with fresh and crenated red blood cells. Total protein was 266 mg. per cent; gold curve 1122100000; mastic 334332; Kahn negative. Urine contained albumin and granular casts. RBC 5.79 million; Hb. 95 per cent. WBC 28,300: 88 per cent polymorphs, 10 per cent lymphocytes, 2 per cent mononuclears. Roentgenograms of the skull demonstrated a marked degree of intrasellar erosion suggesting the presence of a pituitary adenoma (Fig. 1A).

Course. Within a week's time the patient's general condition improved. Fever, confusion, and meningeal signs subsided and the blood disappeared from her spinal fluid, but the ocular findings, viz., the right 3rd nerve palsy and blindness, remained unchanged. After she had recovered sufficiently, carotid angiography was done (on the 24th hospital day) in order to differentiate between bleeding aneurysm and pituitary tumor. This procedure showed no anomaly of the vascular tree of the carotid, and therefore the presumptive diagnosis was made of chromophobe pituitary adenoma with hemorrhage spilling into the subarachnoid space.

Operation. On her 26th hospital day a right frontal craniotomy disclosed xanthochromic and hemorrhagic discoloration of the orbital surface of the right frontal lobe. The chiasm and optic nerves were displaced by a bluish-black hemorrhagic tumor mass which, on aspiration, yielded no blood. After incision of the capsule, a hemorrhagically infarcted pituitary adenoma was thoroughly removed.

Histologic Examination. There were scattered foci of well preserved chromophobe pituitary adenoma with large areas of complete ischemic infarction, old and fresh hemorrhages, hemosiderin deposits, and areas of infiltration with polymorphonuclear leukocytes and macrophages (Figs. 2 and 3).

Postoperative course was uneventful, but the patient remained completely blind when discharged on her 40th hospital day. When last heard of, 6 years later, she was still blind and without sense of smell. She had no other subjective complaints and was working as a Dictaphone operator.

Case 2. St. Mary's Hospital, Grand Rapids, Michigan, No. 50-10580. V.K., female, aged 49. Admitted July 15, 1950. Discharged Aug. 16, 1950.

History. This patient had been in good health except for intermittent, bilateral frontotemporal headaches of 10 years' duration. Thirty-six hours prior to admission, a violent bifrontal headache suddenly developed, associated with nausea and vomiting. A few hours later, marked loss of vision occurred in both eyes, particularly in the left, and the left upper eyelid began to droop. The patient's daughter observed that her mother became mildly confused, showed some difficulties in expressing herself, and displayed impairment of memory and lack of concern towards her illness. By the time of admission, headaches and nausea had somewhat abated, but the ocular signs persisted. The patient's menstrual periods had become irregular at age 46, occurring at 3- to 6-month intervals.

Examination. The patient was moderately obese but showed no other constitutional change. She was slightly drowsy, with slowed cerebration, indifferent mood, and impaired memory and judgment. A slight degree of nominal aphasia was present. Temperature was elevated to 103°, but all other vital signs were normal. There was mild rigidity of the neck. The left eye was practically blind, and there was loss of temporal field on the right. Both optic disks showed a mild degree of primary optic atrophy. Complete paralysis of the left 3rd nerve was noted, as well as mild

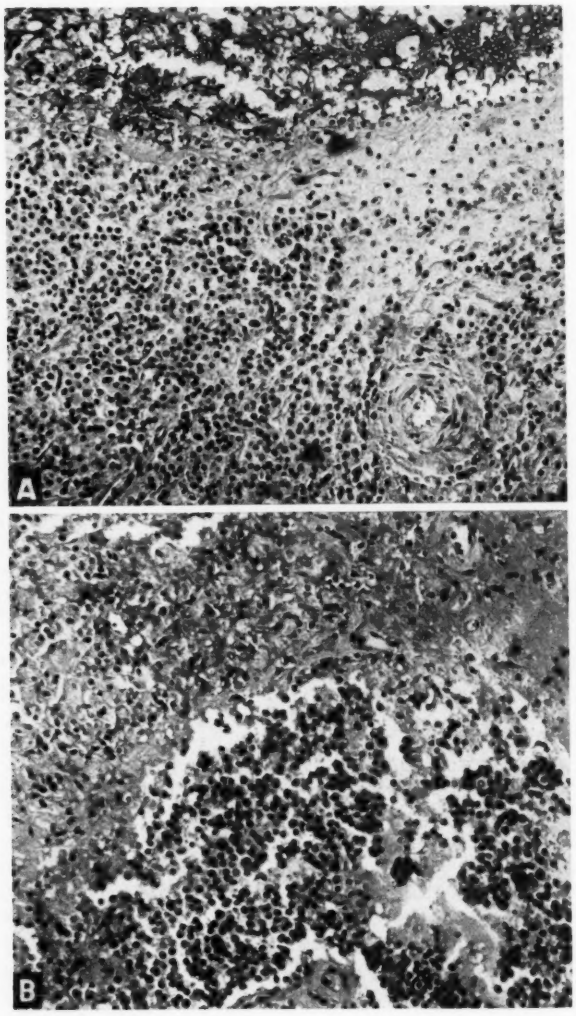

FIG. 2. *Case 1.* Photomicrographs of operative specimen. (A) Pituitary adenoma with sclerotic thick-walled arteriole. Fresh hemorrhage above. (B) Hemorrhage and necrosis with beginning organization above. Adenomatous tissue below.

paresis of the left 4th and 6th nerves. The right upper extremity showed slightly reduced strength with diminished deep reflexes.

A presumptive diagnosis of left carotid aneurysm with subarachnoid hemorrhage was made.

X-rays of the skull showed typical intrasellar type of erosion with barely visible, erect posterior clinoid processes. Since this finding suggested the presence of a pitui-

tary adenoma, the previously planned lumbar puncture was omitted and further laboratory data were obtained. Blood sugar was 109 mg. per cent; glucose tolerance test showed a diabetic curve with elevation to 257 mg. per cent in the first hour and 1+ sugar in the urine. Cholesterol was 207 mg. per cent; B.M.R. was +39.

Course. Within a few days, the meningeal signs subsided and some vision returned in the left temporal field. In consideration of a diagnosis of an aneurysm, left carotid arteriography was performed on the 4th hospital day (Fig. 1 B). This demonstrated no aneurysm, but the parasellar portion of the carotid artery appeared to be a trifle elevated, the siphon stretched, and the terminal supraclinoid portion narrowed with delay of the outflow of contrast medium. The angiogram was compatible with a

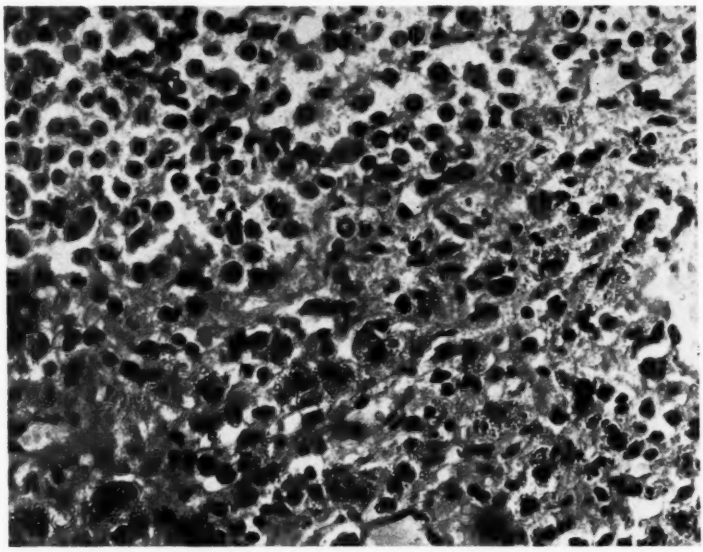

FIG. 3. *Case 1.* Photomicrograph of operative specimen (high magnification). Pituitary adenoma with macrophages containing hemosiderin granules.

diagnosis of a pituitary adenoma, yet it was felt necessary to determine by ventriculography more accurately whether or not there was a supra- or parasellar extension of the tumor. Ventriculograms were normal, ruling out sizable extrasellar extension.

Operation. Because of persistent visual loss and ocular palsies and in the absence of significant signs of hypopituitarism, a left frontal craniotomy was undertaken on the 14th hospital day. A tumor mass was seen to extend underneath the left optic nerve and tract. Old hemorrhage had stained the surface of the left optic nerve. During removal of the tumor an unusual avascular grayish-white appearance of part of the tissue was noted.

Histologic Examination. The specimen proved to be a chromophobe adenoma with marked secondary changes indicative of infarction. There were areas of necrosis, and other areas of old and fresh hemorrhage. The cells of the adenoma had undergone considerable degenerative changes, and in certain places there was marked infiltration with inflammatory cells and young fibroblasts.

Postoperative course was uneventful except for transient euphoric indifference and confusion, but on discharge (31st hospital day) the mental changes had practically disappeared. There was residual right homonymous hemianopsia. The paralysis of the 3rd nerve had started to improve and the function of the 4th and 6th nerves was normal. B.P., and fluid intake and output were normal. Subsequent laboratory studies 6 months later showed B.M.R. −30, glucose tolerance test normal, cholesterol 142 mg. per cent, urinary 17-ketosteroids 13.2 mg. per cent, serum potassium 20.4 mg. per cent, and normal eosinophil response to adrenalin and A.C.T.H. Since hypophyseal function was considered adequate, deep x-ray therapy was given, totaling a tumor dose of 1620 r. When last seen, she was mentally normal and without complaints. Incomplete right homonymous hemianopsia and very slight paresis of the left 3rd nerve were still demonstrable.

Case 3. Blodgett Memorial Hospital, Grand Rapids, Michigan, No. 86887. E. I., male, aged 56. Admitted Aug. 22, 1947. Discharged Oct. 4, 1947.

History. Twenty-four hours prior to admission, the patient suddenly had violent bilateral frontoparietal headaches associated with nausea and vomiting and a feeling of exhaustion. He had had, for the past 15 years, occasional attacks of right-sided headaches which were diagnosed as migraine. His past record revealed no other significant factors except for a history of a subtotal thyroidectomy in 1944.

Examination. The patient was a moderately obese man with a pale, pasty skin. He was slightly drowsy and confused, and had occasional difficulty in expressing himself. Temperature was elevated to 102–103°, but other vital signs were normal. Moderate nuchal rigidity was noted. Eyegrounds and gross visual fields were normal.

A tentative diagnosis of spontaneous subarachnoid hemorrhage was made. On spinal tap, the fluid was pinkish and under pressure of 240 mm.; it contained 1025 crenated RBC; 48 WBC; total protein was 101.7 mg. per cent; sugar 49.5 mg. per cent.

Roentgenograms of the skull revealed a considerable degree of intrasellar erosion with elongated thinned posterior clinoids and ballooned floor of the sella* (Fig. 1 C). This unexpected finding posed new diagnostic problems: Did this patient have a bleeding basal aneurysm which had eroded the sella, did he have a hemorrhage into an unsuspected pituitary adenoma, or was this perhaps a combination of both conditions?

Course. His rather unusual course helped to clarify the situation. After the signs of meningeal irritation had subsided, carotid angiography was planned, but a new dramatic development forced us to forego this procedure. On the 11th hospital day, after a sustained gradual improvement, the patient went into profound shock. His color became ashen, his systolic blood pressure dropped to 60, there was nausea, weakness and drowsiness, and his blood sugar level, which was previously found to be 148 mg. per cent, sank to 58 mg. per cent. Plasma chlorides were 400 mg. per cent. This syndrome suggested acute adrenal insufficiency (Addisonian crisis). Immediate specific therapy (adrenal cortex extract, intravenous glucose in saline) was instituted, followed by prompt improvement. However, milder relapses occurred, each responding to the same therapy.

During all this time the patient exhibited extreme lassitude, was confused and

* Of interest were skull x-rays, later made available, dated 1935 and 1944. The former showed a normal sella, the latter early ballooning.

drowsy, and had occasional paranoid delusions. Furthermore, he complained of blurred vision and diplopia. Repeated neurologic examination disclosed merely a mild paresis of the left inferior rectus but no changes in his vision or visual fields. It was evident that his precarious state precluded drastic diagnostic or surgical measures. The profound systemic reaction was interpreted as acute hypopituitarism produced by hemorrhage and infarction into an almost asymptomatic pituitary adenoma, leading to the secondary symptoms of adrenal insufficiency. The more recent ocular signs were thought to indicate possible pressure of the expanded adenoma on neighboring structures. In order to prevent progression of eye signs, roentgen-ray therapy of the pituitary gland was reluctantly started. On the day of the second x-ray treatment the patient again became desperately ill with peripheral vascular collapse, nausea, and vomiting; but again he responded to adrenal cortex therapy, glucose and saline, which was continued throughout his hospital stay. Further cautious irradiation was well tolerated, until, after 28 days, a total tumor dose of 1446 r was reached. The patient improved slowly and diplopia, visual blurring, and mental changes disappeared, and he was discharged.

The patient was maintained with daily intramuscular desoxycorticosterone acetate in a dose of 3.5 mg., supplemented with methyl testosterone 20 mg., thyroid extract 130 mg., ascorbic acid 200 mg., and a high salt, high protein, high carbohydrate diet with interval and bedtime feedings. He became fully active and returned to work on this regime but further increase in well-being was noted when cortisone orally in a daily dose of 20 mg. replaced the desoxycorticosterone acetate.

Detailed laboratory data relative to his endocrine status have been obtained on several occasions over the past $3\frac{1}{2}$ years. The Kepler water test was positive in both water excretion and chemical portion with total calculated figure of 20 obtained. Urinary 17-ketosteroids were found to be only 2.5 mg./24 hours on one occasion and 1.9 mg./24 hours on another. Blood cholesterol varied from 224 to 470 mg. per cent. Basal metabolism varied from −25 to −41. Glucose tolerance curve was very low and flat, starting with fasting values of 55 and 60 mg. per cent. A.C.T.H. produced no fall in the circulating eosinophils. Further episodes of acute adrenal insufficiency occurred subsequently, the last one in November 1950 following an acute gastro-intestinal infection. Nevertheless, the patient was maintained in satisfactory endocrine balance on a daily regime of cortisone 20 mg., testosterone and thyroid 0.13 gm. Checkup skull films showed recalcification of the dorsum sellae (Fig. 1D).

CLINICOPATHOLOGIC CONSIDERATIONS

Every neurosurgeon is familiar with the fact that pituitary adenomas are highly vascular tumors which easily become imbibed with blood when traumatized. In postoperative autopsy specimens of large pituitary adenomas, one is often amazed to find the entire tumor mass hemorrhagic, even though the area of surgical interference was very limited. It is not clear what causes a spontaneous vascular accident in a pituitary adenoma but there is reason to believe that the growth rate of neoplastic cells may outstrip their blood supply and that increased intracapsular pressure favors ischemia and thrombosis. Once infarction has occurred, a large portion of the adenoma, or even the entire tumor, becomes a hemorrhagic mass that swells up as rapidly as a soaked sponge. Such sudden increase

of volume and of intracapsular tension produces acute compression of neighboring structures. First of all, the optic nerves, chiasm and optic tract, already impinged by the bulk of the pre-existing adenoma, suffer additional serious damage. Later on, pressure may be exerted extradurally against the structures of the cavernous sinus. If the hemorrhagically infarcted adenoma or actual clot formation extends into the parasellar subarachnoid space, the 3rd nerve is encroached upon intradurally and carotid circulation interfered with. An adjacent pituitary lesion may not only compress the carotid mechanically but may also induce local vasospasm by irritation. Finally, sudden suprasellar expansion of the adenoma may compress the hypothalamic region, jeopardizing its blood supply. It is not surprising that some blood may escape into the basilar subarachnoid space, or that, even in the absence of gross hemorrhage, an infarcted adenoma may set up an inflammatory reaction in the basilar cisterns.

With the knowledge of this pathologic background, the neurologic symptomatology may be better understood. In most cases the syndrome follows a fairly constant train of events. It must be emphasized that the presence of a pituitary adenoma frequently was not even suspected before the acute episode. Most of the patients had surprisingly few and uncharacteristic premonitory symptoms. Perhaps the most striking example is the case described by Dingley.[2] His patient, a man in apparently excellent health, ran after a moving bus, and, after he had boarded, dropped over dead. Autopsy showed as the only abnormal finding, massive hemorrhage in a previously asymptomatic pituitary adenoma. In our own observations the patients merely complained of occasional intermittent headaches but gave no inkling of the presence of an intracranial growth. The onset is always dramatic. The initial signs and symptoms such as violent headache, nausea, vomiting, nuchal rigidity, drowsiness and confusion, and elevation of temperature point to the diagnosis of spontaneous subarachnoid hemorrhage. Indeed, the spinal fluid is usually bloody or may show a mild polymorphonuclear inflammatory reaction. In contrast to the insidious onset of symptoms in the average case of pituitary tumor, signs of local damage to adjacent neural structures develop abruptly. Rapid loss of vision, even total blindness, appears to be characteristic of vascular accident in a pituitary adenoma (Case 1 and Case 2). This is illustrated by the following additional brief observation:

University of Michigan Hospital No. 418703. S.K., male, aged 23. This man experienced, on awakening, sudden loss of vision in the right eye. Several months later there was gradual decrease of vision in the left eye. Operation disclosed a hemorrhagic dark brown cyst in a chromophobe adenoma. Five months postoperatively, the patient again suddenly lost his sight, this time on the left side. When re-operated on, a hemorrhagic cyst was found to have recurred in the residual adenoma.

Acute lesions of the 3rd nerve, less frequently of the 4th and 6th nerves, are likewise common. It must be understood, however, that sudden appear-

ance of these neighborhood signs is not necessarily produced by hemorrhage or infarction, but may merely indicate lateral extension of the tumor (Weinberger, Adler and Grant[9]). Evidence of hemispherical involvement has been reported and was present to some degree in our Case 2. It may be ascribed to an impaired carotid circulation or, in some cases, to direct compression of the hemisphere by clot. Acute damage to the hypothalamus plays at least a contributory role in the development of somnolence, confusion, hyperthermia, and disturbance of vegetative functions; in fact, implication of this vital area adds to the gravity of the clinical course. In the subacute state, the neurologic symptomatology may be complicated by superimposed symptoms and signs of endocrine deficiency (Case 3). A massive vascular accident in the adenoma seriously interferes with hormonal function of the remaining anterior pituitary lobe; thus, acute hypopituitarism (cachexia hypophyseopriva) results with secondary adrenal insufficiency.

DIAGNOSIS

The acute development of the clinical picture suggests at first the presence of bleeding intracranial aneurysm, but that diagnosis is immediately questioned when roentgenographic evidence of intrasellar erosion is discovered. Cases of this type present a strong argument for early routine roentgenograms of the skull regardless of the patient's grave condition. The innocuous x-ray examination offers decisive information before potentially dangerous diagnostic steps (such as lumbar puncture, etc.) are carried out. Nevertheless, evaluation of intrasellar erosion in a comatose patient is difficult as the following observation will demonstrate:

Blodgett Memorial Hospital, Grand Rapids, Michigan, No. 50–7143. J.S., male, aged 52.

This man complained of drowsiness and headaches of 2 weeks' duration, and finally became stuporous. There were signs of minimal left hemiparesis. Roentgenograms of the skull showed marked intrasellar erosion and the calcified pineal body was displaced to the left. With such limited information, a tentative diagnosis was made of pituitary tumor with extrasellar extension and/or possible hemorrhage. The patient died before anything more could be done. At autopsy a walnut-sized chromophobe pituitary adenoma without hemorrhage was found, and in addition, a diffuse glioblastoma of the right insular region and adjacent basilar ganglia with marked edema of the white matter of the hemisphere.

When the roentgenograms in the above case were reviewed, the pineal was seen to be shifted not only to the opposite side but also *downward*, whereas in pituitary tumor with large extrasellar extension one could expect the pineal shift to occur *upward*.

Admittedly, a large carotid aneurysm may produce an asymmetric intrasellar erosion. Carotid angiography therefore is necessary to exclude aneurysm. The arteriogram may show minor deviation of the course and shape of the carotid artery, at times with evidence of impaired intracranial blood flow. Once the possibility of aneurysm has been eliminated and the

diagnosis of pituitary adenoma rendered probable, two further problems must be clarified. First, the presence of neighborhood signs always arouses the suspicion of extrasellar extension. In such a situation, ventriculographic studies, as recommended by Jefferson[5] and White,[10] prove informative, yet judgment is required as to whether the diagnostic aid gained by ventriculography outweighs the risk of the procedure. The second problem is to accomplish as thorough an assay of pituitary function as the patient's precarious condition permits, utilizing the following tests: BMR, blood cholesterol, fasting blood sugar and glucose tolerance, Kepler's water balance test, fluid intake and output, eosinophil response to adrenalin and ACTH, and finally urinary 17-ketosteroid determination. These data furnish an essential base line for further diagnostic and therapeutic management and permit early recognition of panhypopituitarism.

TREATMENT

Management of the acutely ill patient as illustrated in our observations should be conservative and supportive until the signs of subarachnoid hemorrhage have abated. In the meanwhile, laboratory studies will have determined the patient's endocrine status. If definite pituitary deficiency is present, as in our Case 3, surgical diagnostic procedures and operations are clearly contraindicated. Specific endocrine substitution therapy should then be given until hormonal decompensation is controlled. Such medication may have to be continued as a maintenance dose for a long period even after the acute emergency has passed. It is our present opinion that roentgen-ray therapy should not be given immediately after a vascular accident has occurred in a pituitary tumor. In Case 3, for instance, a serious aggravation of signs and symptoms occurred during irradiation which was administered assuming a policy of "calculated risk." This may or may not have been due to this treatment, nevertheless, there are reports in the literature describing sudden onset of vascular accidents in pituitary adenoma while roentgen-ray treatment was under progress (Sosman,[8] Dott, Bailey and Cushing[3]).

In the presence of marked visual loss and paralysis of adjacent cranial nerves, early surgical intervention is indicated, but it is important to possess preoperative information concerning possible extrasellar extension of the tumor. In spite of early evacuation of the infarcted and hemorrhagic pituitary adenoma, damage to the optic nerves and chiasm may prove irreversible (Case 1). Postoperative x-ray therapy should be postponed until endocrine functions have become stabilized.

SUMMARY

Pituitary adenomas occasionally tend to undergo vascular changes such as massive hemorrhage or infarction.

The resulting clinical syndrome is dramatic and puzzling in as much as the adenoma may have previously produced minimal or no symptoms. There is acute onset of grave intracranial signs such as subarachnoid or

intracerebral hemorrhage. Blindness or extra-ocular palsies may rapidly develop. Secondary signs of acute panhypopituitarism (with adrenal insufficiency) frequently complicate the picture. The cerebrospinal fluid is either bloody or may show moderate polymorphonuclear pleocytosis. Roentgenograms of the skull disclose typical intrasellar erosion. Carotid angiography may be required to differentiate the condition from bleeding intracranial aneurysm.

If severe loss of vision or extra-ocular palsies have occurred, early operation is indicated, provided there are no signs of acute hypopituitarism. If, however, the clinical syndrome is dominated by evidence of severe panhypopituitarism surgical treatment is inadvisable and even roentgen-ray treatment dangerous; supportive hormonal therapy should then be given.

Three illustrative cases with good outcome are reported.

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PTERIONAL MENINGIOMAS "EN PLAQUE"

FRANCESCO CASTELLANO, M.D., BENIAMINO GUIDETTI, M.D., AND HERBERT OLIVECRONA, M.D.

Neurosurgical Clinic, Serafimer Hospital, Stockholm, Sweden

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THE present communication deals with sphenoidal ridge meningiomas of the pterional type, with invasive and hyperostotic alterations of the cranial bones, and the results obtained after surgical treatment. The material of verified meningiomas observed in this clinic (Olivecrona[9]) up to Dec. 31, 1946 consists of:

Parasagittal	205
Convexity	91
Sylvian, sphenoidal ridge	111
Gasserian envelopes, basis of middle fossa	17
Olfactory groove	46
Suprasellar	42
Intraventricular	18
Posterior fossa	72
Varia	6
	608

They represent 18.4 per cent of 3256 verified brain tumors.

The sphenoidal ridge meningiomas represent 18.25 per cent of the 608 tumors observed. The sphenoidal ridge may be divided into three portions (Cushing[1]): (1) deep, inner or clinoidal; (2) middle or alar; (3) outer or pterional. The inner two-thirds corresponds to the posterior margin of the lesser sphenoidal wing; the outer third to the flaring margin of the greater wing. The cases in our series are:

(1) deep, inner or clinoidal	15
(2) middle or alar	17
(3) outer or pterional	74
(4) middle fossa	5

The pterional tumors are of two different types: (1) global meningiomas, which usually exceed in diameter their area of attachment and which expand into the fissure of Sylvius; and (2) meningiomas "en plaque," which provoke invasive and hyperostotic alterations of the greater and lesser wing of the sphenoidal bone.

In our series there are:

(1) global	59
(2) "en plaque"	15

To these 15 verified cases must be added 10 other clinically verified cases which have been under observation for several years (since 1938) and in which the slight discomfort did not justify surgical treatment.

INCIDENCE. DURATION OF SYMPTOMS

In our series 19 tumors occurred in women and 6 in men. In Cushing's material 19 tumors occurred exclusively in women. We know of 6 examples reported in men (1 case respectively of Stender,[12] Weskamp,[13] Poppen and Horrax,[11] Milleret[8] and 2 cases of Penfield[10]). The average age proves to be 47 years; the youngest patient was a woman aged 17, the oldest 63 on admission.

The duration of symptoms in verified cases was, on an average, 4 years. But we are of the opinion that the onset passed unobserved for several years, because of the small discomfort. In many cases in which the physical examination and X-ray showed the alterations to be extremely advanced, one was forced to the conclusion that the onset of the disease, even though no symptoms had been observed by the patient, dated back for a considerable time.

SYMPTOMATOLOGY

Unilateral exophthalmos was the most frequent initial complaint. In 11 cases it was recorded as the initial symptom and, in the remaining 14, it developed during the course of the disease. In 4 cases temporal swelling was the first symptom and in 10 cases it developed during the course of the disease. (In 64 cases collected from the literature, exophthalmos was inaugural in 46 patients and temporal swelling in 4 cases. Exophthalmos and temporal swelling were said to have coincided in 8 cases.) In 5 cases headache was the initial symptom and subjective dimness of vision in 4 other patients.

Occipitofrontal headache, more frequently referred to the orbits, was present in 13 cases, with a tendency to lateralization in 4 instances; it was rarely described as severe. In only 2 cases was it accompanied by vomiting.

Convulsions occurred in 4 cases. Two of the patients had suffered only one major attack, 1 had occasional attacks and only 1 had many attacks of generalized convulsions.

Four patients showed slight mental impairment. In 3 cases psychosensory hallucinations were present; in 1, olfactory and gustatory hallucinations; in 1, gustatory hallucinations; and in 1, visual hallucinations in the contralateral visual field and at the same time olfactory hallucinations.

PHYSICAL EXAMINATION

Impairment of olfactory function was noticed in only 4 cases. Fourteen of the patients showed palpable swelling in the temporal region. The unilateral, nonpulsating, irreducible exophthalmos was present in every patient; the eyeball was most often pushed forward and downward and many showed a more or less pronounced oedema of the eyelids. Only 2 had conjunctivitis. In most of the patients the movements of the affected eyeball were limited in all directions, but the limitation was not always directly proportionate to the degree of protrusion of the eyeball. Impairment of sight was present in 15 cases. Two patients had ipsilateral blindness, with

nearly normal contralateral vision. In 4 cases the ipsilateral acuity was greatly reduced with normal contralateral sight, and in the other 9 cases it was moderately reduced. Ten of the patients had normal vision.

In the majority of the cases papilloedema of a slight degree was present; in 7 instances it was ipsilateral. In 4 cases an ipsilateral atrophy and in 2 Foster Kennedy's syndrome were found. In 8 patients the fundus was normal.

In 22 patients the fields of vision were normal. In 2 an ipsilateral temporal defect was present. Oculomotor paresis on the side of the lesion was present in many patients and was doubtless due to implication of the nerves as they pass through the superior orbital fissure.

In 2 patients the trigeminal nerve was affected and in 3 a contralateral lower facial paresis was noticed.

X-RAY

In 24 of the 25 cases X-ray studies made it possible to verify the diagnosis of sphenoidal meningioma "en plaque," and even in the remaining case, in which no pathological changes were reported at the time of examination, a review of the films showed that typical alterations were present. The X-ray films on lateral, anteroposterior and to even better advantage on postero-anterior views, showed a sclerosis of the ala parva, which extends frequently from the pterion as far medially as to the anterior clinoid process. Often it involves also the orbital roof, the floor of the middle fossa, and the greater wing component of the outer wall of the orbit. In 1 case there was an absorption of the sphenoidal ridge. The superior orbital fissure was narrowed in 12 cases and the optic foramen in 2. In 6 cases the foramen spinosum was distinctly wider on the side of the tumor, and in 10 cases at operation it was noted that the middle meningeal artery was hypertrophied. In 2 cases the X-ray showed signs of a general increase in intracranial pressure (erosion of the posterior clinoid processes, of the dorsum sellae and of the floor of the sella turcica). The comparative radiological studies over a long period of time showed that the hyperostosis had grown extremely slowly and in fact almost imperceptibly, as shown in Fig. 1 (Mrs. H. H., History No. 713/42).

ENCEPHALOGRAPHY AND VENTRICULOGRAPHY

In the cases of meningiomas not operated upon, the encephalograms showed little or no ventricular displacement or a slight dislocation. In the verified cases the alterations were a displacement of the anterior part of the ventricular system toward the normal side, varying from 1–10 mm., and a displacement of the tip of the temporal horn backwards, upwards and medially.

"In a certain measure, the amount of extension of the bone change provides better information with regard to the spread of the tumor than does the pneumography. The value of the latter lies perhaps primarily in

the fact that a doubtful bone change may be controlled and, if the patient is not operated upon (as these tumors grow slowly and give slight symptoms at their early stage), the repeated examinations may provide information with regard to the eventual intracranial progress of the lesion" (Lindgren[7]).

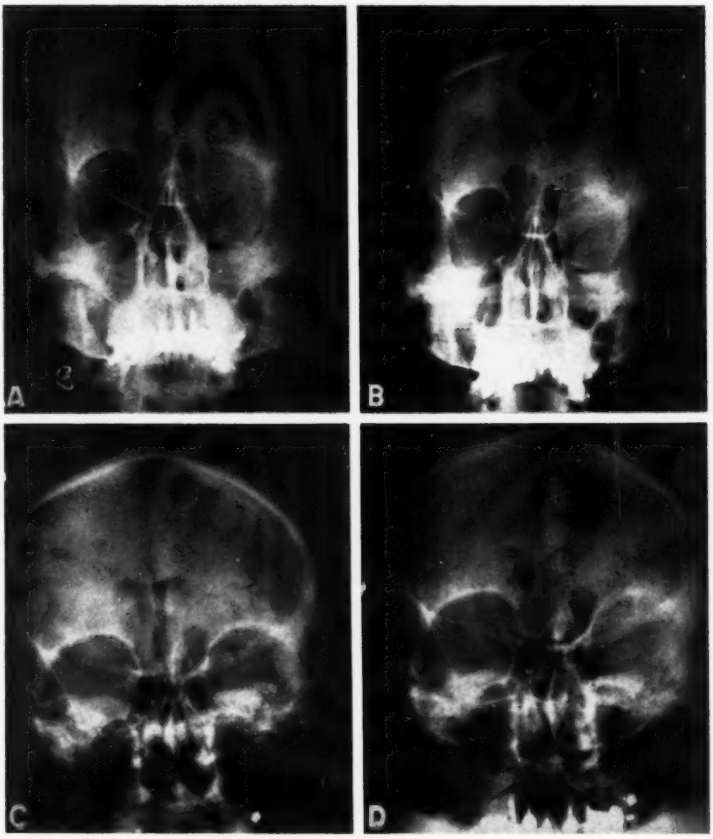

FIG. 1. (A) X-ray 1942. (B) X-ray 1947. (C) Encephalogram 1942. (D) Encephalogram 1947.

PATHOLOGICAL CONSIDERATIONS

The meningioma "en plaque" is a tumor of limited thickness growing along the planes of the meninges, in some cases occupying a considerable area. The relation of the primary tumor to the hyperostosis appears to consist in a relatively insignificant, superficial carpet of subdural tumor, with involvement of the thickened dura and a greater development of the adjacent bone, usually affecting the lesser and greater wings of the sphenoid

and the floor of the middle fossa. The hyperostosed bone frequently attains a thickness of 3 or 4 cm.

Of 15 verified tumors, 2 infiltrated the pterygopalatine muscle and 3 the temporal muscle. In 3 cases the Gasserian ganglion was enveloped; in 2 of these the cavernous sinus was also enveloped and in 1 case the growth had extended through the bone into the orbit.

In 1 case the suspected subdural tumor proved to be a slightly thickened dura, pointing to the possibility of the hyperostosis being primary and unassociated with a subdural lesion.

These tumors differed considerably in vascularity and texture. A large percentage of the meningiomas were of the psammomatous type, which, apparently, has a particular tendency to invade the bone, but there were also other types. One was of angioblastic type and 2 were of malignant type. Invasion of the Haversian canals of the hyperostosed bone was present in 5 cases.

DIAGNOSIS

A diagnosis of pterional meningioma "en plaque" is supported by the following facts:

(1) Occurrence usually in a female of middle age. (2) A history of a slowly developing exophthalmos with ultimate impairment of vision on the affected side. (3) Temporal swelling. (4) Roentgen findings of hyperostosis involving the sphenoidal ridge, the greater and lesser wing of the sphenoidal bone and the roof of the orbit.

Exophthalmos is the most important symptom. It is unilateral, nonpulsating and irreducible, and the eyeball is displaced forward and downward.

In our series of 111 verified and 10 nonverified cases of meningiomas of the sphenoidal ridge, exophthalmos was present in every case of pterional meningioma "en plaque" and in only 5 cases of the other sphenoidal ridge meningiomas. In the series of 64 cases collected from literature it was present in 62 instances.

Unilateral exophthalmos in cases of intracranial tumors has been discussed by Elsberg, Hare and Dyke[2] (1932) and by Ley[6] (1936).

Temporal swelling was present in 14 patients in our series. In the series of 64 cases collected from literature temporal swelling was present in 29 patients.

In all our cases the pre-operative diagnosis was correct.

RESULTS

Operated Cases. In 15 cases there were 2 operative fatalities (13.3 per cent). (Every patient dying in the Clinic is listed as a postoperative fatality.) One patient died 4 days after operation of pulmonary embolism. The other died 2 days after operation from the effects of ligature of the carotid artery.

With regard to the functional results, late and remote, in the group of 13 patients who survived operation, 1 patient died after 35 days of pulmonary abscess; 7 patients were well or had only some defects that did not

seriously affect their earning capacity; 5 patients were unimproved or in worse condition than before operation.

In 6 cases the exophthalmos was improved after operation.

Two patients were operated upon for recurrence 2 years after the first operation. The first died after 7 years from an inoperable continuance of the growth, and the second, operated upon in Lund for an intraorbital extension of the tumor, survived 2 years after enucleation of the globe. Two patients died after about 2 years, from probable continuance of the growth.

The survival period of patients, after leaving the hospital, is shown in Table 1.

TABLE 1

Survival period in 15 verified and 10 unverified cases

Survival Period (years)	Verified Cases		Unverified Cases From First Symptom
	From Operation	From First Symptom	
½–1	12 (R)		
1–2	4 (D)	12 (R)	III (D)
2–3			
3–4			
4–5		9 (F), 4 (D)	X
5–6			
6–7	15		IX
7–8		6 (F), 15	VII
8–9	2 (R), 14	14	
9–10		2 (R)	VI
10–12	11, 13		I
12–15	7, 8, 10	13	II, IV, V
15+	1, 3	1, 3, 5 (F) 7, 8, 10, 11	VIII (24 yrs.)

(R) = death from recurrence.
(F) = operative fatality.
(D) = death from intercurrent disease

Nonoperated Cases. The 10 cases in which the slight clinical discomforts and the little or absent ventricular displacement dissuaded surgical treatment were under observation for several years (1938–1951). Examination of these patients has shown that, except for 2 patients who died from intercurrent disease, the remaining 9 are well and active.

The physical and X-ray examinations after several years showed, except for an increased exophthalmos in 6 cases, stationary conditions or only an extremely slow growth, which was, in fact, almost imperceptible.

The survival period counted from the first symptom is shown in Table 1.

Unfortunately, the literature has recorded only a few cases of pterional meningiomas "en plaque" not operated upon that had been observed during a considerable length of time; on the contrary, there are many cases mentioned in which the dural tumor was not completely extirpated.

Among unverified cases that have been under observation for several years are to be mentioned the 3 in Cushing's[1] series: 1 patient had had a slowly increasing exophthalmos for 31 years; the survival period of the other 2 patients is not specified. Knapp[5] recorded 2 cases: 1 patient was not operated upon and the other was treated only by enucleation, with a survival period of 16 and 18 years respectively. Kirby[4] reported a case with a history of 20 years and Elsberg[2] 1 with a survival period of 21 years.

Among cases in which the dural tumor was not completely extirpated, are to be mentioned Cases 1, 2, 3, 7, 8, 10 and 11 of Cushing's[1] series, in which the survival period from the first symptom was $28\frac{1}{2}$, 25, 30, $13\frac{1}{2}$, $20\frac{1}{2}$, 19 and 5 years respectively (the last patient died from coronary thrombosis); and 1 case of Groff[3] with a history of 20 years.

Unfortunately the majority of the patients had been observed for only a short time.

DISCUSSION

From the observations made in the follow-up study of our cases of hyperostosing meningiomas of the greater and lesser wings of sphenoidal bone, and of all cases collected from the literature, it seems that these patients as a rule should not be operated on and surgical measures should be considered only as a last resort.

There are several reasons for this conservative attitude. In the first place, these tumors grow so imperceptibly slowly that no progress is noticeable even after several years of observation. Consequently, our patients who have not been operated on have been doing just as well as those who have had the tumors removed, and without the risk of attending mortality. Another very important reason for this conservative attitude is that these tumors when they first come under observation practically always have reached a stage where the bone involvement is so extensive that complete removal is technically impossible. Furthermore, the subjective discomforts caused by this type of tumor are rarely of such importance as to justify an operation of such magnitude as would be required to remove all or most of the tumor. It is true that vision on the affected side may be severely impaired or entirely lost and exophthalmos certainly is disfiguring. Nevertheless, even if it were possible to reduce the exophthalmos completely, which the operation, however, rarely does, this hardly seems to be sufficient reason to run the risk of a 10–15 per cent mortality. In addition, the question may be raised whether an attack on the tumor that does not result in complete removal—which, as stated above, is rarely possible—is advisable. New channels for invasion by the tumor of the soft parts, particularly in the orbit and the temporal fossa, may be opened up, thereby leading to very undesirable complications.

The conclusion therefore seems justified that only where there is some considerable intradural extension of the tumor or where unusually severe subjective discomforts are prominent in the clinical picture, should removal of the tumor be considered. The patients should of course be kept under

observation and new encephalograms made from time to time and surgical intervention planned if indications for tumor removal arise, particularly a noticeable growth of the intradural part of the tumor.

If, for one reason or another, operation should be decided upon, the technique used in this clinic is as follows:

General anesthesia is usually necessary because of the proximity of the first or all three of the trigeminal branches. It is usually advisable to close the eyelids by suture, as the postoperative oedema of the orbit may be so pronounced as to increase the exophthalmos to such an extent that the eye is lost. If roentgen studies indicate an increased vascular supply to the bone, preliminary ligation of the external carotid artery might be advisable. A comparatively small temporal flap is usually sufficient. Because of invasion of the bone, the lower half of the flap must frequently be removed. An attempt should then be made to remove all the involved bone before the dura is opened. This part of the procedure may be very difficult because of the extensive thickening of the bone, which makes the use of ordinary bone forceps impossible. In this case, the bone must be burred away with a motor-driven fraise, which is a rather dangerous procedure, as the fraise might slip, particularly when the deeper parts of the sphenoid bone are attacked. In one of our cases this happened and the carotid artery was caught by the burr and torn completely off at its point of entrance into the cranial chamber. This patient died 2 days later from the effects of cerebral ischaemia.

As a rule, the whole of the lesser and greater sphenoidal wings must be removed, together with a large part of the roof of the orbit, which is frequently involved to a considerable extent. In no case, however, have we been sure that all the involved bone had been removed, as the most medial parts of the sphenoidal wings are difficult of access and so close to important structures, such as the optic nerve and the carotid artery, that great caution must be exercised.

After the diseased bone has been removed as far as deemed possible, the dura is opened. The dura involved by the tumor is usually somewhat thickened and there is a thin covering of tumor tissue growing on the inside of the dura. If sufficient bone has been removed, it is usually an easy matter, however, to remove the involved part of the dura. No attempt has been made to cover the defect of the dura and the operation is concluded by replacing such parts of the bone flap as are considered free from tumor invasion.

SUMMARY

This communication deals with 15 surgically verified and 10 clinically verified cases of sphenoidal meningiomas "en plaque" and the special surgical problem as to whether or not they should be operated upon.

The symptomatology, the neurological and X-ray examinations, the present technique, and survival periods in the surgically verified and unverified cases are reported.

The results of this investigation indicate that the hyperostosing meningiomas of the greater and lesser wings of sphenoidal bone that cause only slight subjective complaints and with which no marked displacement of the ventricles can be found, should as a rule not be operated upon and surgical measures should be considered only as a last resort.

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A NEW OPERATION FOR THE RELIEF OF PAIN IN ANGINA PECTORIS

JOHN T. ROBSON, M.D.*
Tacoma, Washington

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SEVERAL years ago the writer became interested in the problems of surgical relief of pain in angina pectoris, and devised a new operative method. This was the subject of a preliminary report in 1948[2] and subsequently has proven to be of lasting benefit.

All operations for this condition now in use are based on the knowledge that pain-bearing afferent fibers from the heart have their cells of origin in the posterior root ganglia of the upper five thoracic spinal nerves, and the fibers may be interrupted at the posterior nerve roots or corresponding thoracic sympathetic ganglia. No operation so far devised relieves pain referred to the head and neck and, in fact, the pain pathways to these areas are not known.

Sympathectomy for cardiac pain was first suggested by François-Franck, and first carried out by Jonnesco. The modern operation consists of sympathetic ganglionectomy of the first three or five thoracic sympathetic ganglia and intervening trunks. White [4] recommends removing only the first three thoracic sympathetic ganglia, but because it has been shown that in some individuals the fourth and fifth ganglia also contain cardiac afferent fibers, and their removal adds little to the difficulty of the operation, most surgeons prefer to remove all five ganglia. Sympathectomy in this manner is effective in abolishing precordial and arm pain homolaterally, and may be used bilaterally when indicated. When pain on the minor side (usually right) is not too extreme it is my practice to operate on one side only as some degree of pain with effort may serve some useful purpose in warning the patient to curtail activity. When the bilateral operation is done, however, patients still retain a sensation of constriction of the pharynx, or flushing of the head and neck as an anginal equivalent, and this sensation may be explained to them as a sign demanding cessation of activities.

Section of the posterior spinal roots of the upper thoracic region was suggested and carried out by Haven and King.[1] The operation is effective in relieving cardiac pain, but results in a band of anesthesia across the thorax and extending onto the medial surface of the arm. The operation requires laminectomy and in the words of White, "this is a more mutilating and dangerous procedure [than sympathectomy]. It is to be recommended only for the neurosurgeon who is well accustomed to spinal operations, but who has not had the necessary technical experience with paravertebral

* Medical Arts Building, Tacoma 2, Washington.

exposure and resection of the ganglia." Formerly I was in agreement with this, but now, as will be discussed later, I consider posterior root section a useful operation.

For completeness it should be mentioned that total thyroidectomy, surgical myocardial revascularization, and so-called pericoronary neurectomy[1] have been used in patients with cardiac pain, but without noteworthy success.

Sympathectomy and posterior spinal root section, while being uniformly effective in abolishing cardiac pain, are also accompanied by some undesirable changes. Denervation of the first five thoracic dermatomes by posterior root section is obviously not desirable in many instances. Sympathectomy, while producing no cutaneous denervation, results in cessation of sweating and in vasodilatation of the upper thorax, upper extremity, and head and neck, and ocular changes characterized as Horner's syndrome. The ptosis, constricted pupil, and enophthalmos of Horner's syndrome, while merely undesirable cosmetic effects, are frequently of great psychic discomfort to the patient. In addition to this, however, the ocular vascular engorgement accompanying Horner's syndrome may precipitate glaucoma or light up an unrecognized chronic glaucoma. The recent interest in stellate blocks for cerebrovascular thrombosis has shown that increased intraocular tension is a constant accompaniment of this procedure, and clinical glaucoma is not uncommon.

DESCRIPTION OF OPERATION

The operation that is the subject of this paper was conceived to provide sensory denervation of the heart without Horner's syndrome or cutaneous anesthesia.

The operation consists of resection of the 2nd, 3rd, 4th, and 5th thoracic sympathetic ganglia with careful preservation of the 1st thoracic or stellate ganglia, and the extraspinal section of the 1st thoracic posterior root. The 3rd, and, if desired, the 4th rib is approached by a muscle-splitting incision 5 cm. to one side of the corresponding spinous process, and 3 cm. of the vertebral end of the rib are resected as in the Smithwick operation. The transverse process of the vertebra is rongeured away and the sympathetic chain exposed extrapleurally. The chain is then resected from just above the 2nd thoracic ganglion to a point just below the 5th thoracic ganglion. Without further rib resection, the 1st thoracic nerve is identified and traced to where it emerges from the foramen. The nutrient spinal artery can frequently be identified and separated to one side. With gentle traction on the nerve the posterior root ganglia can be brought into view in the foramen, and with a blunt right-angle hook the anterior and posterior roots identified at their junction. With gentle traction still maintained a right-angle Adson ganglion knife can be slipped into this aperture, and the posterior root sectioned just proximal to the dorsal root ganglion. The operation is then completed with closure and aspiration of epipleural air. The operation in the upright position is not difficult but, in my experience, in the prone position it can be very time-consuming.

The patient who was the subject of the preliminary report,[2] was a 51-year-old housewife with a 4-year history of angina and 6 months of angina decubitus. All medical efforts at pain control were without effect insofar as allowing return to any activity. Medical findings revealed no systemic disease other than hypertension, and EKG findings were those of left axis deviation and horizontal heart position only. It was felt that there was reasonable life expectancy and therefore surgery was recommended and carried out March 25, 1948. The patient has been observed over $3\frac{1}{2}$ years and results are gratifying. She is able to be up and about and do minimal housework without precordial or extremity pain. Exertion and emotion, however, are accompanied by facial flushing and feeling of constriction in the pharynx, and serve to keep the patient's activities within bounds. There is no demonstrable cutaneous hypesthesia, ptosis or constriction of the pupils. The skin does not sweat over the left upper thorax, arm and head and neck.

The ocular changes of Horner's syndrome are referable to resection of the first thoracic ganglia and this is avoided in the operation described. There is no clinical recognition of hypesthesia from the interruption of the first thoracic dorsal nerve root.

It is my practice in the surgery of angina pectoris to use the operation described in all cases in which there is predominantly unilateral pain. The operation is safe, rapid and effective. In patients with pain that is severe bilaterally, however, I use laminectomy and dorsal root section as I believe it is of less hazard than a two-stage paravertebral operation in patients with cardiac disease.

SUMMARY

A new operation for the pain of angina pectoris is described. It consists of resection of the second, third, fourth and fifth thoracic sympathetic ganglia and division extraspinally of the first thoracic dorsal nerve root. This operation is without the undesirable side-effects of other operations now in use.

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THE POSSIBLE USE OF NEUTRON-CAPTURING ISOTOPES SUCH AS BORON[10] IN THE TREATMENT OF NEOPLASMS

1. INTRACRANIAL TUMORS*

WILLIAM H. SWEET, M.D., AND MANUCHER JAVID, M.D.†

Department of Surgery, Massachusetts General Hospital, and the Harvard Medical School, Boston, Massachusetts

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OUR purpose here is to describe the first exploratory steps we have taken in man leading to the use of a beam of slow neutrons from a nuclear reactor (atomic pile) in an effort to improve the treatment of neoplasms. The nuclei of certain atoms have a pronounced tendency to capture these slow neutrons, breaking down and yielding lethal amounts of energy. We propose to indicate how this energy may perhaps be channeled usefully to destroy tumors.

Efforts to accomplish this by energies liberated at nuclear disintegration of radioactive isotopes have to date been discouraging except in radioactive treatment of metastases of carcinoma of the thyroid. The problem of making the isotope concentrate in the tumor to a usefully greater degree than in any other cells of the body is the one that has not yet been solved. The rapidly metabolizing hepatic cells, the gastro-intestinal mucosal cells, the white blood cells and precursors of the red blood cells all appear to take up intravenously injected isotopes about as fast as, or even faster than malignant tumors. When enormous differentials were found in radioactive P^{32} uptake between intracranial tumors and normal brain[9] it was at first hoped that this might lead to useful therapy since the high energy β particles (electrons) emitted by the decaying P^{32} could travel only a few millimeters in tissue and their destructive effect in the head would hence be confined largely to tumor, sparing most of the normal brain. However, as Table 1 shows, liver and bone marrow take up as much or more P^{32} than does a malignant glioma. In our hands and those of Erikson and Steelman,[2] P^{32} has in fact not proven helpful as thus far used in the treatment of brain tumors since the neoplastic cells have not shown a greater sensitivity to β radiation than the normal cells of liver and bone marrow.

The formidable character of the barrier between blood and normal brain as contrasted with the much more permeable barrier between blood and brain tumor is also attested to by studies with K^{42} (Selverstone, Sweet and Ireton)[10] and I^{131} in diiodofluorescein (Moore *et al.*).[4] At optimum times

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† Clinical Research Fellow in Surgery.

after intravenous injection K^{42} may be found in intracranial tumors at concentrations exceeding 100 times those in normal white matter and diiodofluorescein may concentrate up to 29 times as much in brain tumors as in normal brain.

It would appear that we can utilize this difference between the blood-brain and the blood-brain tumor barrier if we can find some stable atom which will concentrate in a brain tumor but which can then be made to disintegrate by an appropriate neutron radiation confined to the head and yielding large amounts of energy in the head only. The amounts of this special atom elsewhere in the body would be immaterial since other areas would be outside the destroying ionizing effect of the neutron beam. The

TABLE 1

Activity ratios of tissues at autopsy

Case number	9	13	16
Hours, injection to death	57.3	62.2	364
Tissue	Activity Ratio		
Glioblastoma	29.9	54.2	5.5
Blood	—	—	1.8
Skeletal Muscle	26.7	15.5	2.6
Canc. bone with marrow	48.6	56.5	4.4
Spleen	41.0	29.9	7.3
Liver	87.6	60.9	10.1

intracranial gliomas and meningiomas are likely candidates for this form of attack since with few exceptions they do not grow elsewhere in the body and since the treatment of gliomas is notoriously in need of improvement.

It was indicated as early as 1940 both by Kruger[3] and by Zahl *et al.*[13] that substances that yield energetic atomic particles when they capture very slow (thermal) neutrons might be useful in the treatment of cancer. Among the requirements for advancement in this direction are: (1) An adequate source of slow neutrons. (2) A method for distributing throughout tumor but not normal tissue an isotope that avidly captures neutrons. (3) Determination of the absolute concentration of such an isotope in various tissues that would be required to enable a neutron beam of given intensity to kill the neoplastic cells but spare the normal ones. The intense flux of neutrons required is now available at the nuclear reactor at the Brookhaven National Laboratories. Before indicating our efforts regarding steps 2 and 3 we shall summarize some of the pertinent facts of nuclear physics and biology.

Most of the nuclear radiations, i.e. gamma rays, beta particles, alpha particles (helium atoms with a double positive charge), protons and fast neutrons, are usually produced at radioactive decay with large energies ranging up into a few millions of electron volts (mev). When rays or particles at these high energies react with

matter dissipating their energies, the net result is the displacement of orbital electrons ionizing the remaining atom, with a potentially lethal effect on neighboring living tissue. These reactions are relatively nonspecific and most of the atoms of matter participate in them. Although the neutrons arising in the nuclear reactor as the consequence of the fission of uranium are given off at high speeds, their velocity can be reduced by collisions within graphite or heavy water until the thermal neutron range is reached. Furthermore since the neutron carries no electrical charge it wanders more freely in matter than do the charged particles.

However, thermal neutrons, those whose speed has been cut down to about 2200 meters/sec., leaving them with an energy of only .025 electron volts (ev), interact with matter in an entirely different and much more specific fashion. Their energy, and that of the so-called epithermal neutrons moving somewhat faster, is insufficient to produce ionization since of the order of 10 electron volts is required to displace an orbital electron. Neutrons at these lower energies react with the atoms in living tissues largely by undergoing capture by the nuclei of certain of the atoms they meet.

An atomic nucleus that has captured a neutron becomes a new compound nucleus with an excess of energy which it immediately gives up in one of two major ways by:

(1) Emission of a capture radiation (gamma ray or heavy particle) forming a stable isotope.

$$\text{hydrogen}^1+\text{neutron}\rightarrow[\text{hydrogen}^2]\rightarrow\text{hydrogen}^2+\text{gamma ray}$$
$$H^1+n\rightarrow[H^2]\rightarrow H^2+\gamma(2.23\text{ mev})$$
$$\text{boron}^{10}+\text{neutron}\rightarrow[\text{boron}^{11}]\rightarrow\text{lithium}^7+\text{alpha particle}$$
$$B^{10}+n\rightarrow[B^{11}]\rightarrow Li^7+\alpha^{++}(2.4\text{ mev})$$

(2) Emission of a capture radiation (gamma ray or heavy particle—in the example below, a proton), forming a radioactive daughter which then continues to emit a further radiation at its characteristic rate.

$$\text{nitrogen}^{14}+n\rightarrow[\text{nitrogen}^{15}]\rightarrow\text{proton}+\text{carbon}^{14}\xrightarrow[5700\text{ years}]{\text{half life}}\text{nitrogen}^{14}+\text{electron}$$

$$N^{14}+n\rightarrow[N^{15}]\rightarrow p^+ + C^{14}\rightarrow N^{14}+\beta^-$$

Both the immediate "capture" radiations and the "decay" radiations from any radioactive daughter are ionizing and capable of producing a biologic effect which must be estimated for every type of atom within any tissue to be irradiated with slow neutrons.

The potential usefulness of such radiations depends upon the remarkable eagerness of a few unusual isotopes to capture slow neutrons while all of the common naturally occurring elements in living tissue tend relatively to ignore them. The avidity of an isotope for absorption of slow neutrons is expressed as its capture cross section σ_a, the apparent area in cm.^{2} presented by a single nucleus of the element to an incident beam of neutrons, = "barns" $\times 10^{-24}$ cm^2. The σ_a for the main elements in normal tissue is as follows: H = .32, N = 2.15, O = < .001, P = .23, Cl = 40, Na = .45, C = .0045, Mg = .3, S = .4, K = 2.5, Ca = .5. In contrast with these low values are those for a limited number of isotopes among all the others to be found in matter. Thus Li^6 = 870; B^{10} = 3900; Cd^{113} = 24,000; Sa^{149} = 46,000; Eu^{155} = 14,000; Gd^{157} = 200,000; Dy^{164} = 2620; Hg^{199} = 2500.

Of these isotopes with a high σ_a our first choice has been boron[10] because its carefully worked out toxicity permits large doses intravenously in man, and its capture radiation is an alpha particle which at its energy of 2.4 mev travels only about 14μ in tissue. Hence its destructive effect will be limited either to the cell containing the parent atom of B^{10} or to the cells in its immediate vicinity.

Our results to date suggest that boron may be given intravenously in man in a form that will concentrate in brain tumors to a clinically useful degree. We have given i.v. to 23 adults with brain tumor 5.0 g. of borax

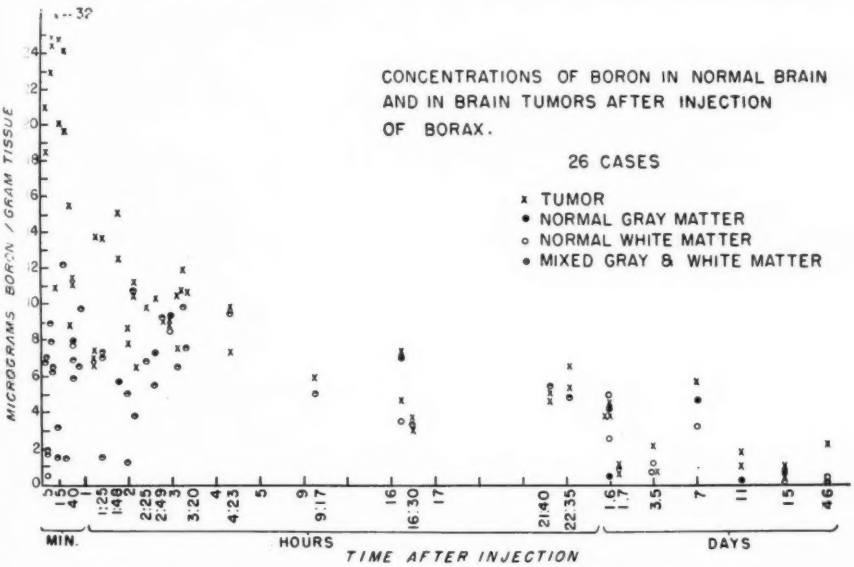

FIG. 1. Determinations recorded on the same ordinate all come from the same patient. In 6 patients multiple groups of analyses at different time intervals are recorded. In 3 patients with glioblastomas whose autopsic analyses at 1.6, 11 and 15 days are recorded, borax plus glycerol was injected; in the remaining 23 patients borax alone was injected. Tumor types represented include 13 cases of glioblastoma, 5 of astrocytoma, 3 of hemangioblastoma, 2 of metastatic carcinoma, and 1 each of melanoma, meningioma and chordoma.

($Na_2B_4O_7 \cdot 10H_2O$), containing 0.57 g. of boron. In another 35 patients the injected agent contained 6.3 g. of glycerol to each 5.0 g. of borax. A loose bond is said to be formed between the two and we hoped that this might diminish their entry into normal brain but not into neoplasm. At the time of operative removal of the brain tumor, specimens were taken of this and of nearly normal gray and/or white matter and frequently of scalp, muscle, bone, blood and cerebrospinal fluid. The boron content of each type of tissue was determined by the colorimetric method of Ellis, Zook and Baudisch, using 1–1[1] dianthrimide. With more vigorous digestion of the tissue and the use of 200–500 mg. samples, this method worked out for plants

proved suitable for human material. Both the Beckmann spectrophotometer and the Evelyn colorimeter were used to read the color densities.

The resulting data have been plotted in the figures. Fig. 1 reveals that, when specimens of neoplastic and normal tissue were taken from 5 min.

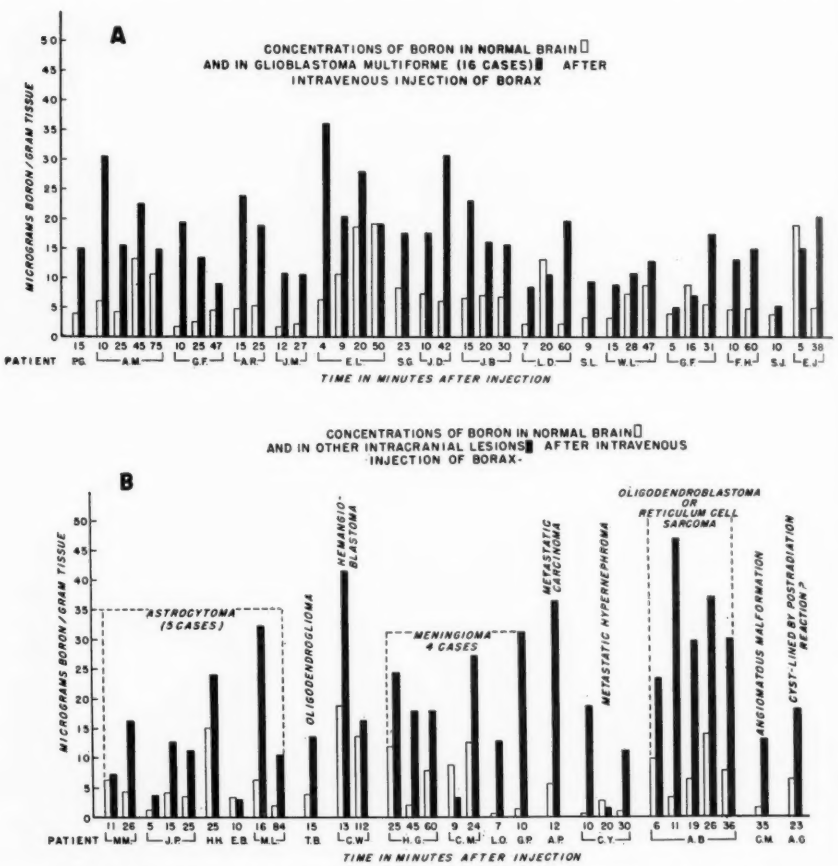

FIG. 2. The patients of (A) and (B) received an aqueous solution containing 5 g. borax and 6.3 g. glycerol/70 kg. body weight.

up to 46 days after the intravenous injection, ratios of tumor to normal reaching 3 to 1 occurred rarely after the first 30 minutes. The absolute concentrations as well as the ratios also dropped rapidly to of the order of $\frac{1}{2}$ of the highest levels by 2 hours and finally down to 2 micrograms or less/g. of tissue after 10 days. This figure of $1\frac{1}{2}$ weeks would appear tentatively to be the shortest interval at which a treatment could fruitfully be repeated.

As soon as we became convinced that the first 30 minutes represented the most probable time at which useful ratios were to be found we concentrated our specimens in this period and took several at different times from many patients in an effort to define more precisely the brief duration of the highest tumor:brain differential. In Fig. 2A we see the results in our 16 cases of glioblastoma multiforme both for normal and tumor at each pair of specimens, and in Fig 2B the data for the other 7 types of tumor represented and for two other kinds of lesion are plotted in similar fashion. In

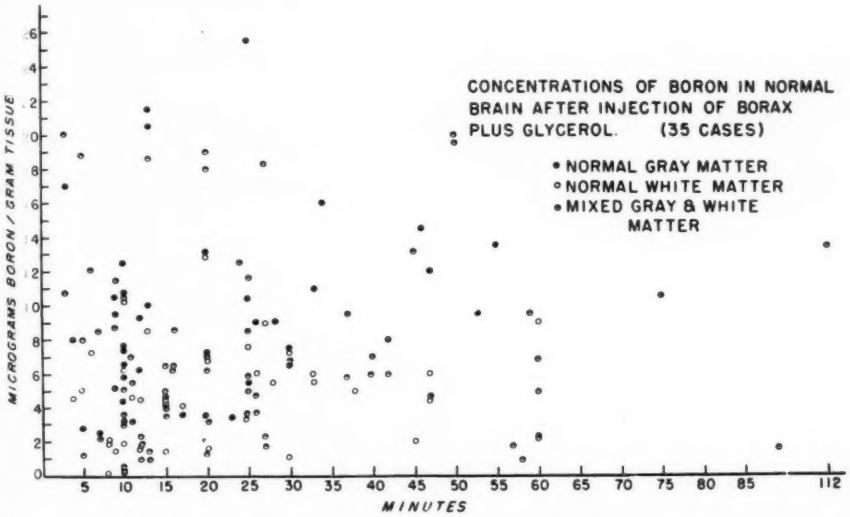

FIG. 3. Each circle represents a single determination on a specimen presumed to be normal.

the glioblastoma group one notes that there is no constant pattern of rise or fall in boron concentration in either the tumor or the normal tissue. However, in 7 of the cases a high absolute concentration in tumor at a level over 3 times that in normal tissue was found at or before 20 minutes following injection. A maximum ratio, tumor: white matter of 48:1, was seen at 10 minutes in one case. In Fig. 2B one sees that the two patients with metastatic malignancy, the oligodendroblastoma, one of the astrocytomas and two of the meningiomas followed this same pattern. The other slowly growing tumors showed poorer ratios. We are seeking other compounds of boron that will yield more protracted better differentials over a wider range of tumors. The data show considerable fluctuation in the concentration of boron in the various presumably normal specimens. In the 35 patients from whom samples of normal brain were obtained after injection of borax plus glycerol (32 of them represented in the histograms of Fig. 2) one sees in Fig. 3 such variation in values that curves to represent the

average for gray and for white matter would have little meaning. Since nearly all of the so-called normal specimens have come from areas close to frank tumor, there may be some degree of breakdown of the blood-normal brain barrier in some of these specimens. Aliquot specimens for histologic study are now being taken routinely and have at times shown that tissue thought on inspection to be normal was neoplastic and vice versa. The variability of our present data precludes our being able to draw a standard curve for the uptake in normal brain. However, about two-thirds of the

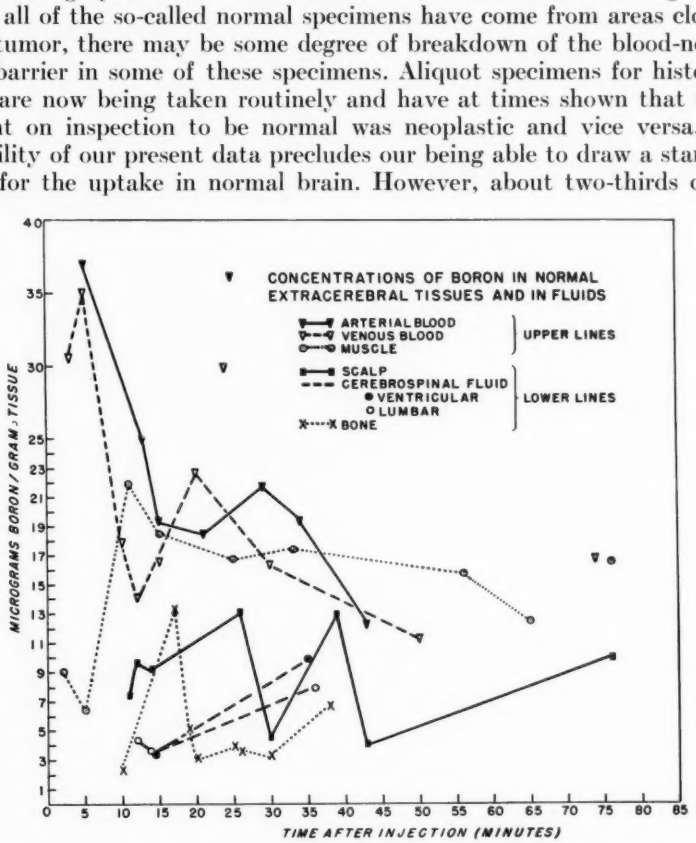

FIG. 4. Each point represents the average of several determinations from different patients on the particular type of specimen at the time interval noted. The figures from which the averages were taken were often widely disparate.

determinations lie below 8μg./g., with the gray matter slightly above the white.

A summary of the results of analysis for boron in other tissues and fluids is shown in Fig. 4. We were particularly anxious to know the concentrations in blood lest the high concentrations in malignant tumors in the first 20 minutes be explicable largely on the basis of their greater blood content. However after 5 minutes the concentrations in both arterial and venous blood are of the same order of magnitude that one often sees in the rapidly growing tumors, i.e., 15–25 μg. B/g. tissue. Hence it is the tumor itself that is taking up the boron. (No grossly bloody specimens of any tissue were analyzed.) Uptake in scalp is fortunately relatively low so

that this important layer would be likely to survive the neutron bombardment. The amounts in muscle and bone are unimportant from the standpoint of survival of these tissues, but one needs to know the amount therein in order to compute the percentage of the neutron beam they would absorb.

One encouraging feature of these data is the relatively high concentration of boron throughout brain and tumor with such a small nontoxic dose. Since a craniotomy was either being or shortly to be performed, no effort was made in these cases to move the dose up into the maximal range consistent with recovery. But since the patient will not have to surmount an operation at the time he is being exposed to the neutron beam, the dose of boron just prior to exposure can, if necessary, be pushed even to slightly dangerous levels to secure a maximal therapeutic effect. We have given intravenously to several adults with brain tumor 15 g. borax/70 kg. body weight and have found this to be well tolerated. If subsequent work indicates that even larger doses would be fruitful we could use as an antidote to toxic effects a 1:1 plasma, Ringer's solution i.v., since Pfeiffer, Hallman and Gersh[8] found this a more protective regime than any other they tried in experiments on acute toxicity of boric acid in animals. We have calculated the effects of the thermal neutrons on the assumption that a 15 g. dose of borax would be used and would yield 3 times as much boron in the tissues as the 5 g. dose has done.

For our calculation of the ionizing effect of the neutron beam we have selected concentrations of 50 micrograms of B^{10}/g. of tumor, 15 μg./g of normal gray matter, and 10 μg./g of normal white matter. These figures will probably be higher with a 15 g. dose of borax in most cases. We have also assumed use of a borax specially synthesized from B^{10} with the high capture cross section of 3900.

Our estimation of the concentration of boron necessary to make the locus of this element the major determinant of the ionizing effect follows the lead of Conger and Giles[1] who irradiated with slow neutrons the buds of the plant *tradescantia*. If one excludes contamination by fast neutrons or gamma rays from the same source yielding the slow neutrons, then ionization occurs only when the thermal neutrons are captured and comes from: (1) radiations arising at the time of capture—notably in hydrogen, nitrogen and boron, and (2) emanations from any radioactive isotopes formed. In the human head, only chlorine, sodium and phosphorus form radioactive daughters that could possibly contribute significantly to the radiation.

The energy of ionization per unit time per unit volume of tissue for each element therein = $F \times N \times \sigma_a \times E \times A$, in which F = flux, number of thermal neutrons crossing a cm.^{2} per second; N = number of atoms of an element per unit volume; σ_a = the capture or absorption cross section, the area in cm^2 presented by a single nucleus of the element to the beam of slow neutrons; E = energy in a million electron volts of radiations emitted after the capture of the neutron; A = the fraction of this emitted energy absorbed in the tissue.

Details of the computation from this and other pertinent formulas are

being published elsewhere (Javid, Brownell and Sweet). The results indicate that at the concentration of B^{10} of 50 μg./g. in tumor and 15 μg./g. in normal brain—a ratio of 3.3:1—the evolved energy in tumor will be 3 times that in the normal, so that this amount of B^{10} in the tissues suffices to make its precise locus the significant determinant of the total radiation effect.

We also need to know the relative sensitivities to radiation of normal cerebral tissue and of each neoplastic type or subtype. Data on this point from x-ray therapy in man are conflicting. Sosman[11] has had one case of verified glioma treated during 18 months with a total depth dose measured roughly at 6000 r. The patient died 7 years postoperatively from the radiation, postmortem examination showing destruction of the glioma and of much normal brain as well. O'Connell and Brunschwig[5] found a similar state at necropsy in one of their previously gliomatous patients who had received the same dose. Wachowski and Chenault[12] found diffuse severe cerebral damage in 6 patients given doses to neoplasm of 6000–9000 r; some living tumor cells remained, however, in each of the 3 patients in this group who came to autopsy. Peirce and Bouchard,[6] on the other hand, allege that their standard minimum tumor dose of 7500–9000 r has produced no clinical or cytologic evidence of damage to normal brain. Even more massive doses have destroyed all of large tumors and fatal amounts of normal brain (Pennybacker[7]).

In contradistinction to X-rays, a beam of slow neutrons is rapidly reduced in intensity as it travels through tissue. We have calculated the diffusion length of thermal neutrons (the distance at which the beam will be reduced to 1/e ($\frac{1}{2.718}$) of its original intensity as 2.3 cm. for brain containing 12 μg./g. of B^{10}. This may be compared with 2.85 cm., the diffusion length of thermal neutrons in water, and roughly 2500 cm. in air. We propose to make direct measurements of many points in an irradiated brain in order to establish with greater certainty the distribution of the ionization. In view of this reduction in the neutron beam, however, it appears advisable to use it for treatment in the first instance in patients whose solitary brain tumor has already been subtotally or even grossly totally removed. Some time after recovery from the immediate effects of operation, the cerebrospinal fluid is withdrawn from the head, including the bed previously occupied by the tumor. Replacement of this fluid with air should permit the neutrons almost direct access to that part of the brain that still contains neoplastic remnants, and the injection of B^{10} shortly before exposure to the neutron beam may be followed by differential destruction of the rest of the neoplasm.

The impetus to carry out these studies was provided by the work of Conger and Giles;[1] we now present an effort to transfer directly to the brain of man conclusions drawn from data in plants. If this proves feasible it will be because of the atomic nuclear level at which the interactions occur.

SUMMARY

Certain isotopes, such as B^{10} have a special tendency to capture slow

(thermal) neutrons, whereas the atoms normally present in living tissues do not do so. Since B^{10} at capture yields an alpha particle of high energy which travels only about 14μ in tissue, the site of the atom of B^{10} determines the site of destruction of tissue following this capture reaction. Chemical analyses in 58 cases after intravenous injection of borax show that this concentrates in many rapidly growing brain tumors to more than three times the extent that it does in normal brain. This differential is maintained for only the first 20–30 minutes after injection in most cases. The total amount of boron that may be introduced without toxic effects yields concentrations in tumor $>50\mu$g./g. and in brain $>15\mu$g./g. of tissue—sufficient, according to our computations, to cause, despite other capture reactions, energy in tumor three times that in normal tissue. A tactic for utilizing these effects to treat brain tumors in man is described.

We are pleased to acknowledge the tremendous assistance given to us in the prosecution of this work by Professor A. Baird Hastings.

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CASE REPORTS AND TECHNICAL NOTES

APOPLEXY IN A PITUITARY CHROMOPHOBE ADENOMA

PRODUCING THE SYNDROME OF MIDDLE CEREBRAL ARTERY THROMBOSIS

CASE REPORT

MAX T. SCHNITKER, M.D.,* AND HARLEY B. LEHNERT, M.D.
Toledo, Ohio

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The syndrome of pituitary apoplexy due to degenerative changes in adenomas of the pituitary body is a relatively rare condition that usually manifests itself by sudden onset of oculomotor nerve palsies, coma and bloody cerebrospinal fluid.

In a recent review of the subject Brougham, Heusner and Adams[1] summarized 7 cases reported in the literature, and gave a detailed analysis of 5 additional cases from their own series. The clinical diagnosis is difficult as shown by the fact that in 10 of the 12 cases it was made only at autopsy. The treatment is likewise unsatisfactory, for as the authors pointed out, 2 of the 12 patients survived on expectant treatment and only 2[3,6] survived immediate surgery.

The following case is reported because the clinical manifestation of the pituitary apoplexy was quite unlike the picture as presented in the literature. In our case it was the typical picture of thrombosis of the middle cerebral artery in a patient with a known old pituitary chromophobe adenoma.

CASE REPORT

G. M., male, aged 65, was admitted to Flower Hospital, Oct. 10, 1949 with paralysis of the left side of sudden onset. In 1938 he had had a verified chromophobe adenoma of the pituitary operated upon by Dr. Max Peet. There had been no recent symptoms of headaches or failing vision to suggest a recurrence of the tumor. He was feeling well until October 9 when he suddenly fell to the floor at home and was found to be paralyzed on his left side and unconscious.

Examination. He was a well nourished and developed elderly man with a "pasty" appearance consistent with a hypopituitary habitus. Cooperation was only fair due to his stuporous state. Head was normal with a well healed right transfrontal craniotomy scar. The neck was moderately rigid. There was questionable anosmia. The optic discs were flat and chalky white with a sharp border indicative of primary atrophy of long standing. There was bitemporal hemianopsia by confrontation. The pupils were round and equal and reacted to light and accommodation. The extra-ocular movements were full and without diplopia or nystagmus. Corneal reflexes and facial sensation were normal. There was a left lower facial weakness. The remaining cranial nerves were normal. There was complete flaccid paralysis of the left arm and leg with edema of the left wrist and ankle. Tendon reflexes were hypoactive on the left. Abdominal reflexes were absent. Babinski sign was positive on the left. Sensory examination showed hypoesthesia and hypoalgesia of the entire left side. The heart was moderately enlarged with a precordial mid-diastolic rumble. B.P. was 130/80. There were a few rales at the lung bases. The abdomen was negative.

Laboratory Findings. Lumbar CSF was clear and at 120 mm. pressure. Fluid analysis showed 7 lymphocytes and total protein 50 mg. per cent. Blood count was 3.4 million; Hb. 71 per cent; WBC normal. Urine was cloudy with 10 mg. quantitative albumin.

* 1031 Secor Hotel Building, Toledo 4, Ohio.

Skull x-rays Oct. 12, 1949 showed the old osteoplastic flap in good position. There was marked "ballooning" of the pituitary fossa, measuring 23×21 mm. The dorsum sellae was thin and the posterior clinoids were absent.

Clinical Diagnosis. On the basis of the history of onset, neurological and spinal fluid findings, a working diagnosis of thrombosis of the right middle cerebral artery was made.

Course. A right stellate ganglion block was carried out 18 hours after the initial catastrophe with 20 cc. of 1 per cent novocain. A very good Horner's syndrome was produced on the right side and within 5 minutes he was able to lift his left arm and leg off the bed. On the following morning he still had some movement of the left side. Another right stellate ganglion block was done, but without improvement. Two days later the patient became more drowsy and left hemiplegia returned. There was no change in ocular signs or other cranial nerves. He became irrational, progressed into deepening coma and expired Oct. 25, 1949, 15 days after admission to the hospital.

Autopsy. Gross findings. The body was that of a well nourished elderly white male with very little body hair and the appearance of an eunuch. There were no external deformities

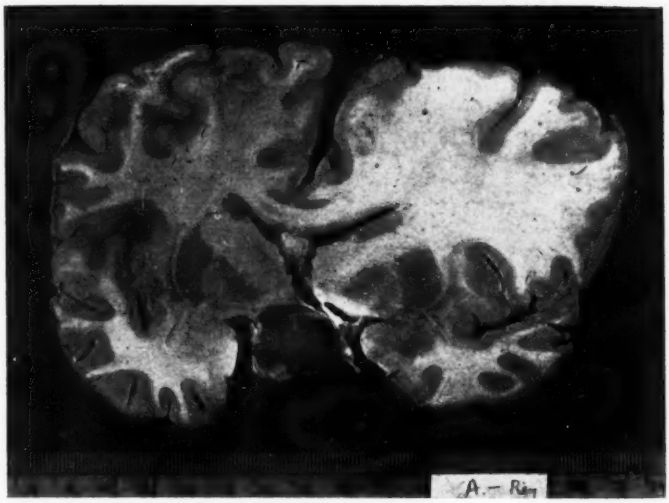

FIG. 1. Coronal section showing hemorrhage into the pituitary body.

other than the old right frontal craniotomy scar. The dura was adherent to the right frontal lobe, which showed yellow-brown discoloration and thinning of the cortex. The pituitary body proper was transformed into a large gray, fairly soft new growth measuring 4 cm. in its widest diameter. It protruded considerably above the roof of the sella and contained a fairly recent hemorrhage, especially on the right side (Fig. 1). The optic chiasm was atrophied and stretched over the tumor. The tumor impinged upon the midbrain without any invasion of the brain or sella turcica.

On section of the brain the right hemisphere was found to contain an extensive area of encephalomalacia, particularly the anterior portion. Grossly, the encephalomalacia was demarcated anteriorly at a level of the tip of the anterior horn of the right lateral ventricle and extended posteriorly to a vertical plane passed through the vestibulum of the right lateral ventricle. In depth it extended from the midline to the lobus insularis laterally.

On opening the arteries that comprise the circle of Willis, there was noted slight arteriosclerotic thickening, but no obstruction of the lumen anywhere. There was, however, a

marked compression of the right middle cerebral artery and, to a lesser extent, the right anterior cerebral artery by the pituitary tumor which was expanded by the hematoma within its capsule. The encephalomalacia in the right hemisphere was in the area of blood supply of the right middle cerebral artery and seems therefore to have been caused by the compression of the arteries.

Microscopic findings. Brain: Sections from the area of encephalomalacia, taken from the olfactory area and internal and external capsule of the right hemisphere, show extensive necrosis of brain tissue. Sections from the right frontal lobe show atrophy and scarring of the cortex. No significant changes were found in brain tissue distant from the lesions.

Pituitary: The tumor (Fig. 2) is composed of uniform-appearing cells arranged in cords separated by sinusoidal spaces (sinusoidal type).[5] There are numerous thin-walled and rather wide blood vessels between the cords of cells, indicating considerable vascularity. A portion of the section includes the edge of recent and extensive hemorrhage with great extravasation

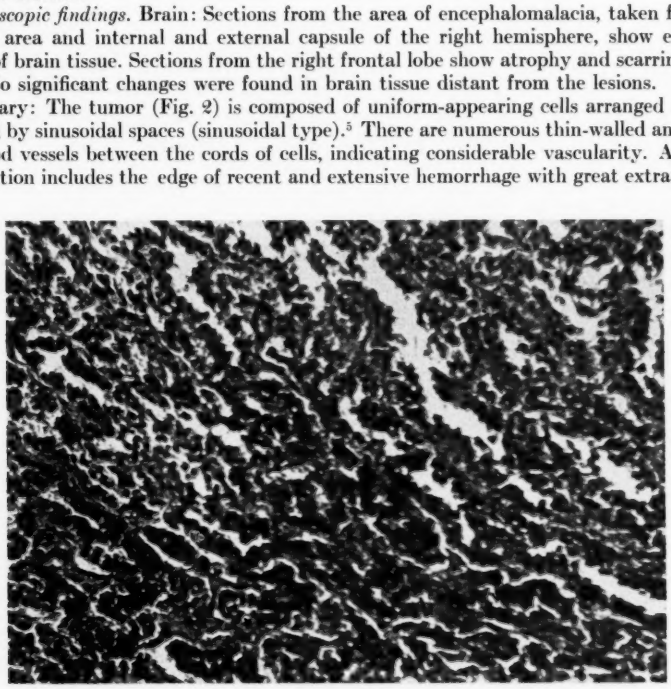

FIG. 2. Photomicrograph. Chromophobe adenoma of pituitary (sinusoidal type).

of red cells into the tumor. The connective tissue is quite variable. In some areas there are heavy septa which form an interlacing framework, while in other areas the interstitial connective-tissue element is hardly discernible. The cytoplasm took a neutrophil stain and is rather pale and free from granules. The nuclei show slight variations in size and shape and are vesicular, normal or oval. Mitotic figures are infrequent and not atypical. Degenerative changes are slight, with some vacuolization but no necrobiosis.

Pathological Diagnosis. (1) Pituitary adenoma, chromophobe sinusoidal type, with recent hemorrhage into tumor. (2) Compression of the right middle cerebral artery by the hemorrhage into the pituitary tumor. (3) Extensive infarct with encephalomalacia in the right cerebral hemisphere. (4) Status posteraniotomy (old) with atrophy of right frontal lobe and dural adhesions to the brain. (5) Rheumatic heart disease—chronic; mitral stenosis and insufficiency with cardiac dilatation and chronic passive congestion of the lungs.

DISCUSSION

A number of cases of acute hemorrhage into pituitary tumors were found in isolated reports in the literature. The majority of the patients apparently harbored

unsuspected pituitary adenomas, mostly of the acidophile type and less commonly the chromophobe type. In these cases the diagnoses were made only at autopsy. There were only a few instances of an acute fulminating hemorrhage into a verified adenoma treated previously (Cairns,[2] Jefferson,[4] Cushing[3] and Sosman[6]). Heroic measures of sellar decompression were life-saving procedures and might have saved our patient had it been instituted.

The symptoms of coma, diplopia and ophthalmoplegia were given as the usual clinical picture in pituitary apoplexy. Our case presented transient coma, left hemiplegia and no ocular symptoms whatever. Hence in this individual, aged 65, with sudden coma and a left hemiplegia with clear cerebrospinal fluid, our attention was directed toward the treatment of a thrombosis of the right middle cerebral artery rather than to a pituitary apoplexy in the absence of pituitary neighborhood signs even though we knew he harbored an old chromophobe adenoma.

In a study of the pathological anatomy of chromophobe adenomas of the pituitary body it was found that they can be divided into two fairly distinct groups—the "diffuse" and the "sinusoidal" type. Not only was the cell type the same, but the same arrangement of cells was found throughout a given tumor.[5] In none of the previous reports has any mention been made as to the cell pattern of either of the above two types occurring in cases of pituitary apoplexy. Theoretically one might expect hemorrhage from the delicate capillaries around a cyst, but again there apparently was no cyst in any of the reported cases. Our patient had a solid tumor of sinusoidal type without any evidence of cyst formation.

Had we re-explored the known tumor rather than resorting to stellate ganglion block with novocain on the basis of the clinical picture presented, the outcome would still be conjectural, as pointed out by Jefferson[4]—that "operation on old standing and massive tumors is not often profitable for the patient."

We are indebted to Dr. Theo. Zbinden for the photographic reproductions. Dr. A. E. Rhoden performed the autopsy.

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NEUROGENIC SARCOMA TREATED BY SURGERY AND RADIOTHERAPY

EDWARD S. MURPHY, M.D., WILLIAM R. LIPSCOMB, M.D., AND JOHN S. BOUSLOG, M.D.
Pathology Department, St. Luke's Hospital, Denver, Colorado

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"Neurogenic Sarcoma" is the general heading applied to a group of malignant tumors usually arising from mesodermal elements of nerve trunks. However, Foot[1] and Stout[5] both include the rare malignant neurilemmoma (malignant Schwannoma) under this heading, and the Schwann cells are generally agreed to be of ectodermal origin.[1] Stout further states, though, that this latter tumor is an extremely rare source of the malignant nerve sheath tumors. None of these "neurogenic sarcomas" arise from the nerve fibers proper. Neurogenic sarcomas may arise anywhere along the course of peripheral nerves and are seen most commonly after the age of 30 and about equally in both sexes. It is usually possible to demonstrate the connection of the tumor to a nerve trunk and often the tumor is represented only by a fusiform, diffuse swelling of the nerve. Sometimes infiltration into surrounding soft tissue structures may be demonstrated grossly. The great majority of these neoplasms develop in individuals suffering from von Recklinghausen's disease, although some instances have been reported in individuals apparently not having that disease. All are characterized by persistent growth with a marked tendency to reappear after attempts at removal, and a great many have proved fatal. They are generally considered to be extremely radioresistant.[2,4,5] The heading, "Neurogenic Sarcoma," also includes a small number of tumors exhibiting epithelial elements and which reproduce in a more or less recognizable form embryonal or adult neuroectodermal structures.[3,5] Stout also reports that the neurogenic sarcomas that have been reported as occurring without any evidence of von Recklinghausen's disease show the same clinical and biological behavior as those with the disease; 50 per cent of the operated tumors reappeared locally and 30 per cent had metastasis, usually in the lungs. Fifty per cent of the patients were known to have died of the sarcoma.

CASE REPORT

Mrs. M.M., aged 48, was admitted to St. Luke's Hospital on June 5, 1946 with a chief complaint of pain in the left leg of 8 months' duration. The pain had recently become more severe and almost constant. It originated in the left popliteal space and traveled down the leg and was accompanied by "considerable twitching" of the leg. The past history was non-contributory.

Examination revealed a moderately enlarged heart and edema of the hands and feet. The left leg was flexed at the knee and hip and the posterior thigh muscles were contracted. Tenderness and slight swelling were noted in the left popliteal space. No pulsation was demonstrable. There was analgesia of the lateral and dorsal aspects of the left foot. No reflexes could be elicited in the left lower extremity. The oral temperature was 99.2°F. and the blood pressure, left arm, was 184 systolic, 124 diastolic.

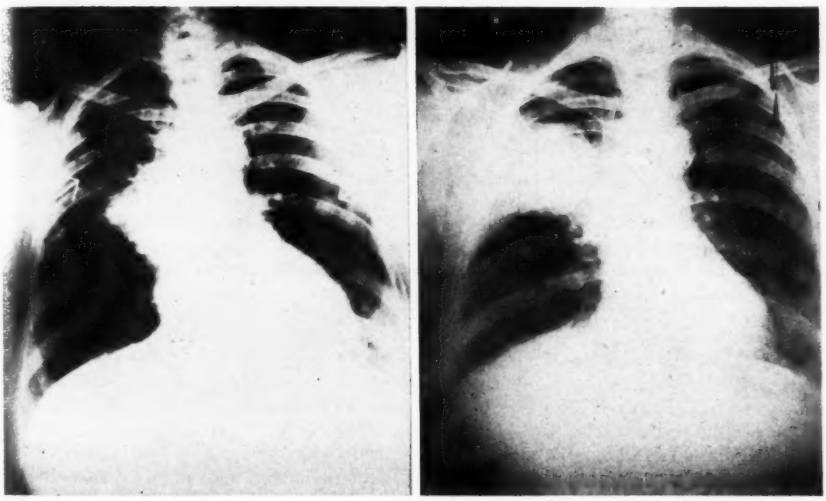
A roentgenogram on June 6, 1946 showed a soft tissue mass in the left popliteal space. The bone was uninvolved except for osteo-arthritis in the knee joint. Blood Kahn test was negative.

Operation. On June 12, 1946, under local anesthesia, the lower third of the thigh posteriorly and popliteal space were explored. The tibial nerve was exposed proximal and distal to the tumor. The tumor was fusiform, 2.5 cm. in diameter, and 3 cm. in length. In removing the tumor it was necessary to resect 6.5 cm. of the nerve. The nerve ends were then dissected

free and an end-to-end anastomosis was accomplished with the leg in a flexed position. The peroneal nerve had become involved in the periphery of the tumor but was easily shelled out from it. Surrounding connective tissue was also cleaned out. A plaster cast was applied from the toes to the gluteal region with the knee flexed at 90°.

Pathological Diagnosis. "Malignant tumor of nerve trunk, structure consistent with either cellular anaplastic neurosarcoma or sympathicoblastoma."

Course. The patient was discharged on June 24, 1946. She was then given the following radiotherapy: Between July 25, 1946 and Aug. 7, 1946 at 400 KV and 70 cm. distance with 2.25 mm. copper filtration, 1482 r (measured in air) was delivered through two ports of the left knee. Between July 30, 1946 and Aug. 6, 1946, with the same physical factors, 741 r was



FIGS. 1 and 2. Roentgenograms of chest. (*Left*) June 25, 1948. (*Right*) Aug. 15, 1949.

delivered to an anterior port, left groin. Then between Sept. 23 and Sept. 27, 1946, again with the same physical factors, 988 r was delivered to two ports at the left knee and between Sept. 24 and Sept. 27, 1946, 494 r was delivered to the anterior port over the left groin.

Second Admission (June 25, 1948 to July 2, 1948). Aged 51. The patient stated that for several days she had experienced pain in the right side of the chest, especially on inspiration, accompanied by cough and hemoptysis, fever and chills, and nausea and vomiting.

Examination. There were râles in both lung bases. There was no evidence of local recurrence in the left popliteal space. A chest roentgenogram on June 25, 1948 "shows a large, rounded mass in the right hilar area. Other smaller spherical dense areas are scattered throughout both lungs. The bones are intact. The left cardiac ventricle is slightly prominent. Impression: Secondary neoplasm deposited throughout both lungs." In Fig. 1 the R. hilar mass is well seen and smaller nodules are seen in the L. 3rd and R. 2nd intercostal spaces.

On June 26, 1948, the sputum contained no acid-fast bacilli.

Course. The patient was treated with antibiotics for a low-grade bronchopneumonia and discharged, symptomatically improved, on July 2, 1948.

She was again given radiotherapy in the following manner: at 200 KV, 50 cm. distance and with 2.25 mm. of aluminum filtration, between Feb. 1 and Feb. 11, 1949, 1984 r was delivered to three ports, anterior R. chest and lateral R. chest.

Between Aug. 17 and Aug. 22, 1949, with the same physical factors, 744 r was delivered

to two ports, anterior and posterior R. chest. Between the same dates and with the same physical factors, 744 r was delivered to two ports, anterior and posterior left knee region.

Third Admission (Aug. 15, 1949 to Sept. 9, 1949). Aged 52. The patient stated that during the past year she had had five or six attacks of "pneumonia," each attack accompanied by hemoptysis and sharp pain over the R. anterior chest wall. She had had no weight loss and her appetite was good.

Examination. There was a tender, egg-shaped mass at the proximal end of the scar on the posterior surface of the left thigh. Chest roentgenogram on Aug. 15, 1949 was read as: "Left lung clear. Cardiac silhouette as before. There is a large, well defined density in the upper portion of the R. lung. It is attached to the lateral chest wall in an infraclavicular region and measures about 8 cm. in largest diameter. Impression: Clearing of many of the metastatic pulmonary processes previously described. Another large single lesion is described in the R. lung at this time" (Fig. 2). A second chest x-ray showed another smaller mass near the R. hilum.

The RBC was 5.3 million and the WBC 10,400 with a normal differential count.

On Aug. 25, 1949 bronchoscopy was done, and "the left main bronchus was explored and found normal. The carina was normal. There was a thickening of the wall of the right main-stem bronchus near the R. upper lobe but no tumor was seen."

Operation. On Aug. 29, 1949 an upper R. lobectomy was done: "On opening the chest a tumor was found, 8 cm. in diameter, adherent to the chest wall and overlying the mediastinum. A smaller, satellite tumor was adherent to the perichondrium. Adhesions were divided and the R. upper lobe freed. Both tumors were in this lobe. A frozen section was read as neurosarcoma. Then the R. upper lobe was removed. No other tumor was palpated or seen in the R. lung."

Pathologic Diagnosis. "Neurogenic sarcoma, R. upper lung lobe."

Fourth Admission (April 1, 1950 to April 7, 1950). Aged 53. The patient stated that in June 1949, she had struck her left thigh in a fall, and 7 to 10 days later noted a small tumor which had since grown to the size of a hen's egg and become slightly tender. This was the same tumor noted on admission in August 1949. She had made a good recovery from the lobectomy of Aug. 29, 1949.

Operation. On April 3, 1950, under local anesthesia, the upper part of the old scar on the left thigh, including the tumor and some biceps femoris muscle were widely removed. The recurrent tumor was apparently not attached to any nerve.

Pathologic Diagnosis. "Neurogenic sarcoma, left leg."

Fifth Admission (June 21, 1951 to June 22, 1951). Aged 54. The patient had been symptom-free until June 17, 1951, when she suddenly became unconscious. She was treated in another hospital, and then transferred to St. Luke's Hospital.

Course. Reflexes were absent on the right side. She continued comatose and expired quietly on June 22, 1951.

Autopsy. Evidence of a cerebral thrombosis with concomitant encephalomalacia was found. A small nodule of tumor tissue, not exceeding 2 cm. in greatest dimension, was found in the upper lobe, L. lung.

Histologic Studies. A review of the microscopic sections of the tumor from each of the four occasions on which it was submitted shows an interesting variation in the cell type and arrangement. In sections of the tumor removed from the left popliteal space on June 12, 1946, the pattern is pleomorphic, with areas of swirling, interlacing bundles of narrow spindle cells with fusiform nuclei and scant cytoplasm. These areas alternate with more heterogeneous patterns, in which round, polyhedral and fusiform cells are sprinkled with tumor giant cells having several, usually clumped hyperchromatic nuclei (Fig. 3). This tumor is quite vascular and contains regions of necrosis and hemorrhage. The intercellular substance is scanty and fibrillary. The structure is very cellular throughout and mitotic figures are frequently seen.

Sections from the tumors removed at lobectomy on Aug. 29, 1949 show essentially the same picture, with plump, spheroidal cells being more prominent than the fusiform type (Fig. 4). Mitoses are numerous. There is a slight suggestion of a "basket-weave" pattern. Tumor giant cells are practically absent.

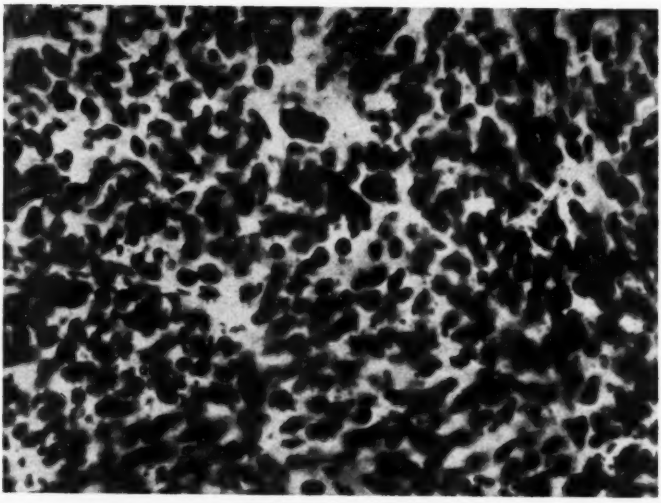


FIG. 3. Neurogenic sarcoma, thigh, first excision, showing heterogeneous pattern with tumor giant cells. (×220)

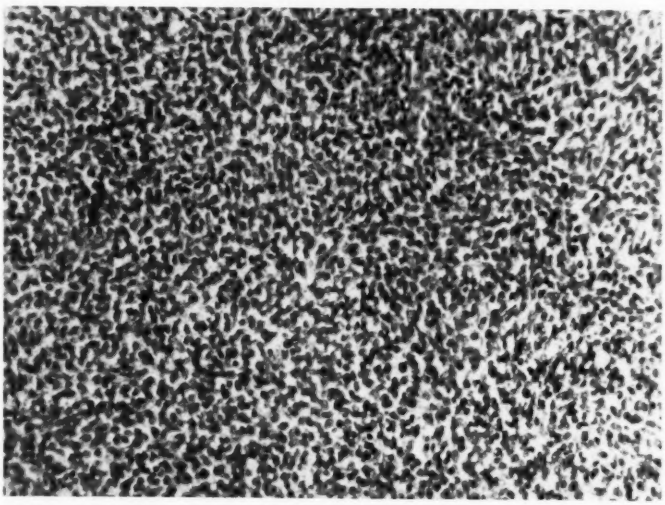


FIG. 4. Metastatic lung tumor removed by lobectomy, showing plump spindle cells in poorly defined "basket-weave" pattern. (×100)

Sections from the nodule of recurrent tumor removed from the left thigh on April 3, 1950 show a pattern in which fasiculation is very prominent and the cell type is almost exclusively fusiform (Fig. 5). The "basket-weave" pattern stressed by Ewing is very well seen in these sections. Mitoses are quite frequently encountered. Tumor giant cells are rarely seen.

Sections from the small nodule of tumor found in the left lung at autopsy show a very cellular, vascular pattern in which the cell type is plump and spheroidal. Occasional fusiform cells are seen. The intercellular substance is scanty.

DISCUSSION

A review of the literature of the past two decades on neurogenic sarcoma and a study of the case that we are now reporting serve to re-emphasize the malignant growth characteristics of these tumors. Their tendency to reappear after attempts at removal is coupled with the quite general accord that they are radioresistant. In the present communication attention has been drawn to the rather wide range through which the cell type and structural arrangement of these tumors can vary. In our case the "basket-weave" pattern was well defined in sections from only one

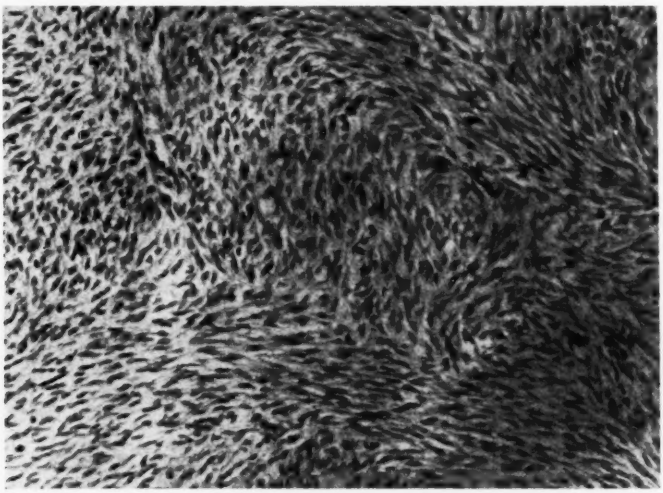


FIG. 5. Section of recurrent tumor of thigh, showing spindle cells with well defined "basket-weave" pattern. (×100)

of the four tumor excisions. We have also noted that in this case of neurogenic sarcoma radiotherapy to metastatic lesions in the right lung was followed by apparent disappearance of tumor nodules in the left lung. This phenomenon has not been infrequently observed in the treatment of metastatic malignancy by radiotherapy.

We do not believe that the small neoplastic nodule found in the left lung at autopsy contributed to the immediate cause of death. The combination of roentgen therapy with surgery had extended the life of this patient in a satisfactory manner until her death was brought about by other causes. This case indicates that in at least some neurogenic sarcomas, radiotherapy in conjunction with surgery is clinically effective.

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CYST OF A CEREBRAL HEMISPHERE TREATED BY INTRAVENTRICULAR DRAINAGE

DOUGLAS MILLER, M.B.*
Sydney, Australia

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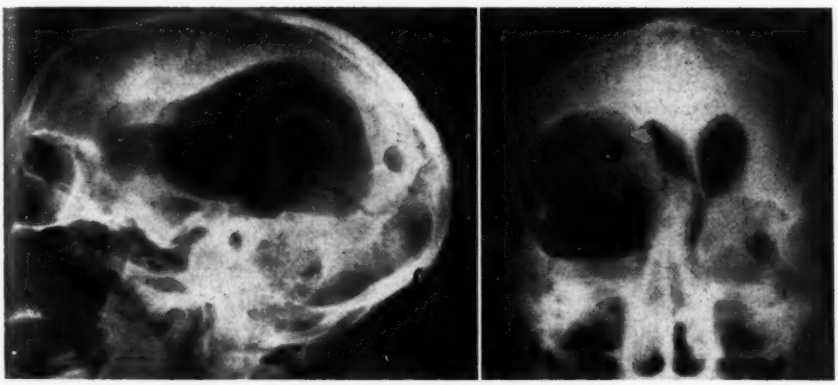
It is now 8 years since a large cerebral cyst of unknown pathology, at the time responsible for symptoms of extreme intracranial pressure, was drained into the lateral ventricle. The patient has remained well, and the artificial opening has kept patent, a communication still existing between a cystic space and the ventricular system.

The case is considered to be of unusual interest both from the speculative point of view as to pathology and because of the satisfactory result of a simple form of treatment.

CASE REPORT

The patient was a soldier aged 23 who was well developed and had been quite well until 9 months before admission. During this period he had suffered frontal headache of increasing severity, and at time of admission this was intense.



FIGS. 1 and 2. Ventriculograms before operation.

During the same period he had gradually lost the vision in his left eye, which had become practically blind. More recently his right eye had suffered severely.

During the previous 6 months he had suffered occasional attacks of an uncinate nature described as unpleasant smells and vague indescribably remote memories.

Examination. He was found to have bilateral high-grade papilloedema; perception of light only was present in the left eye and finger counting only in the right eye. There was a slight sustained tremor of the right arm. Otherwise his central nervous system was normal.

X-rays showed some destruction of the clinoid processes. Lumbar puncture pressure was over 400 mm. water; the fluid was normal.

* 185 Macquarie Street, Sydney, Australia.

FIG. 3. Encephalogram 6 years after intraventricular drainage of cyst.

In view of the paucity of signs a pre operative diagnosis of a midline lesion was made.

At ventriculography a large high-pressure ventricle was entered on the right and on the left a cyst containing several hundred cc. of pale yellow fluid. This fluid did not clot on standing.

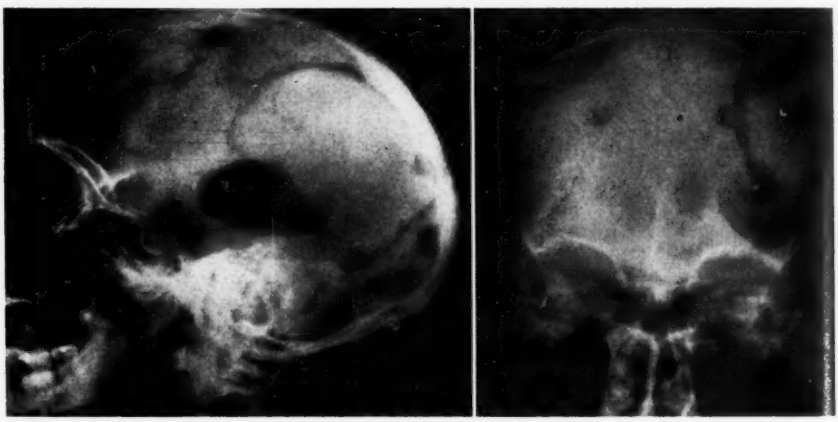
Ventriculograms showed a very large cyst situated in the left parieto-occipital region and occupying most of this part of the hemisphere. There was considerable displacement of the right ventricle (Figs. 1 and 2).

Operation. A large parieto-occipital bone flap was turned down, the dura opened and the cystic cavity found at a depth of 3 cm. from the surface. The cortex was incised and lighted retractors were introduced into the cavity, whose walls could be seen well. The cyst lining was uniformly glistening and smooth, with no suggestion of neoplastic excrescence.

A brain cannula, passed through the medial wall of the cyst, struck the ventricle after passing through about 5 mm. of tissue. This communication was enlarged.

No protein estimation was made of the fluid from the cyst at time of operation as the operation was performed under army service conditions.

Course. He made a good recovery except for permanent and almost complete loss of vision. He is well rehabilitated and leads a useful life. He suffers occasional epileptic seizures.



FIGS. 4 and 5. Encephalograms. Air in cyst after posturing.

A recent encephalogram showed a normal ventricular system still communicating with the cystic space in the left hemisphere (Figs. 3, 4 and 5).

His CSF contained 50 mg. of protein.

SUMMARY

A case of a large hemispherical cyst of unknown pathology is reported.

It presented with anomalous clinical features. It was treated by simple intraventricular drainage. Encephalograms made 8 years later show the communication still in existence.

CASE REPORT OF AN ADAMANTINOMA PRESENT AT BIRTH

C. G. Subramani Iyer, M.D.*

Neurological Unit, Boston City Hospital, and the Department of Neurology, Harvard Medical School, Boston, Massachusetts

(Received for publication October 23, 1951)

A perusual of the available literature has not revealed any instance of the presence of a pituitary adamantinoma at birth. The following remarkable case is therefore placed on record.

Clinical History. The patient M., a girl, was the sixth child born to a mother whose prenatal history was not remarkable. The mother's blood was Rh positive. X-rays before birth revealed a very large fetal head. The mother was admitted to Boston City Hospital in labor on Mar. 1, 1951 with a B.P. of 140/100 and edema of the ankles. Urinalysis revealed 2+ albumin. In order to facilitate birth a lumbar puncture needle was inserted through the top of the presenting head into the lateral ventricle and xanthochromic fluid was permitted to drip out for about 2 hours. This reduced the head to approximately a third of its previous size and delivery was effected by low transverse caesarian section.

Examination. At birth the baby breathed normally and was noted to be in good condition. The heart rate and rhythm were normal and color of the skin was good. The head was markedly enlarged, somewhat asymmetrically with a parietal bulging on the left. The left parietal and temporal bones were extremely thin. Bilateral proptosis and lateral nystagmus were noted. The Moro reflex was sluggish; the deep tendon reflexes were all obtained and there was fanning of the toes on stroking the feet. The cry was high-pitched. The weight of the child at birth was recorded as 8 lbs. 14½ oz.

Laboratory Data. Hb. was 14.5 gm./100 cc.; RBC 7.6 million; WBC 6550/c.mm., with 43 per cent neutrophilic leucocytes, 46 per cent lymphocytes and 11 per cent eosinophils. Occasional nucleated erythrocytes were seen in the blood smear. The platelets appeared normal. The CSF 5 days after birth was slightly xanthochromic; protein was 40 mg. and chloride 690 mg. per cent. There were 260 red cells and no leucocytes/c.mm. of fluid. The sugar value was reported as too low to read. The ventricular fluid was also xanthochromic, with 2000 mg. of protein and 642 mg. of chloride/100 cc. There were 320 red cells and no leucocytes/c.mm. of fluid. The sugar was again reported as too low to read. Radiographs of the head showed a marked expansion of the skull in all dimensions, consistent with hydrocephalus. In one film (anteroposterior projection) a round patch of increased density to the right of the midline was observed.

Course. A few days after birth the baby became deeply jaundiced but this cleared up rapidly. Subsequent ophthalmoscopic examination revealed pale optic discs bilaterally; the disc margins were well defined and there was no trace of papilledema. During the following weeks there was a progressive enlargement of the head and all four extremities became spastic. Throughout the patient's life, all of which was spent in hospital, the temperature was normal, except for occasional elevations to 100°F. and depressions to 95°F. The child died at the age of 3 months.

* Rockefeller Foundation Fellow from Indian Council of Medical Research, Neuropathology Unit, Tata Memorial Hospital, Bombay, India.

Postmortem Examination. Autopsy was performed approximately 24 hours after death The body was poorly developed and emaciated and was in striking contrast to the enormous size of the head. The circumference of the head was 59 cm. Scanty hair was present over the head and the fontanelles were found to be unusually wide and bulging. The pupils were equal and measured 5 mm. The gums were edentulous and the navel was well healed. The length of the body was 55 cm. and the approximate weight was 15 lbs. There were no significant abnormalities outside of the central nervous system. Microscopic examination of the liver and

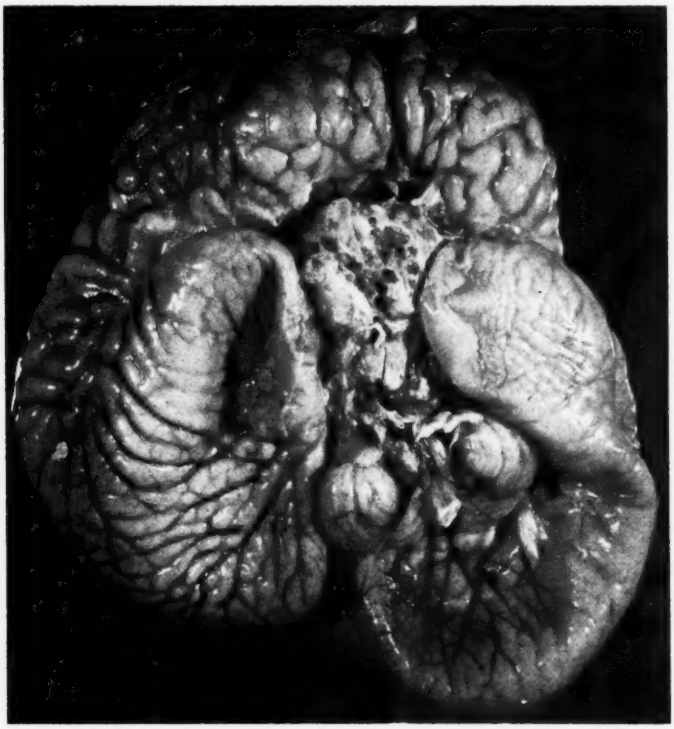


FIG. 1. View of base of the brain to show the extent of the tumor.

spleen revealed large amounts of hemosiderin in the Kupffer cells and the histiocytes respectively. A few cells containing the same pigment were found in the interstitial tissues of the kidneys.

Neuropathological Findings. The dura mater was unusually thick and white over the superolateral surface of the brain. The cerebral hemispheres were large and finely convoluted. Over the occipital and temporal poles the cortex was paper-thin. At the base of the brain there were several moderately dense fibrinous adhesions between the dura and arachnoid. A firm mass presented on the inferior surface of the cerebral hemispheres in the midline encroaching upon the orbital plates of the frontal bones and obscuring from view the vessels and nerves at the base. It was found to arise from the region of the sella turcica and was firmly embedded in the base of the skull. The pituitary body was not found; it had apparently been destroyed by the mass. At the base of the brain (Fig. 1) the mass extended from the posterior third of the orbital surfaces of the frontal lobes to the anterior border of the pons.

The tumor had replaced the structures in the hypothalamic region and had grown into the 3rd ventricle and upper midbrain. The olfactory and optic nerves were destroyed by the tumor and the anterior part of the circle of Willis was stretched over its anterior aspect. The other cranial nerves were normal, and the pons and cerebellum did not appear remarkable.

A series of coronal sections through the cerebral hemispheres revealed the cortex to be considerably reduced in thickness and the lateral and 3rd ventricles to be enormously dilated (Fig. 2). The tumor had grown into the 3rd ventricle, invaginating the floor of that cavity and widely separating the basal ganglia. It extended from the level of the head of the caudate nucleus to the upper midbrain tegmentum. Transverse sections through the midbrain re-

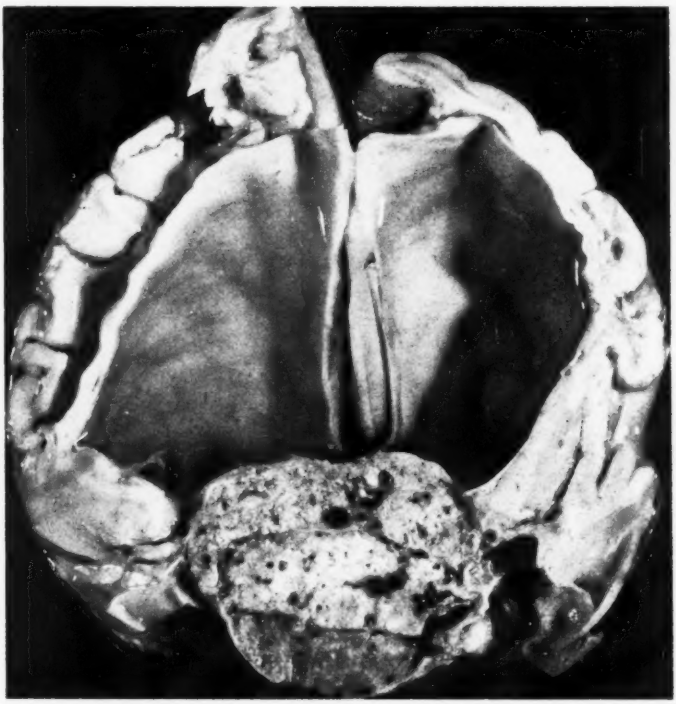


FIG. 2. Coronal section at level of the middle of the basal ganglia. Note the dilatation of the lateral ventricles and the tumor encroaching into the 3rd ventricle.

vealed flattening and wide separation of the cerebral peduncles and obstruction of the aqueduct of Sylvius. The rest of the brain stem and cerebellum were not remarkable.

The cut surface of the tumor had a faintly lobulated appearance. The tumor substance was firm, yellowish-white to pink in color, and calcified in several places. Numerous cysts were present; some of these were lined by tough membrane and filled with glairy mucoid fluid. The tumor had a thin but distinct capsule which surrounded its lateral and anterior aspects.

Microscopic Examination. The tumor was composed of numerous interlacing cords and columns of epithelial cells infiltrating a glial and connective-tissue stroma (Fig. 3A). Many of the epithelial columns had been cut in a transverse plane and showed a peripheral layer of tall columnar cells (Fig. 3B) placed upon a basement membrane. These cells had a fair amount

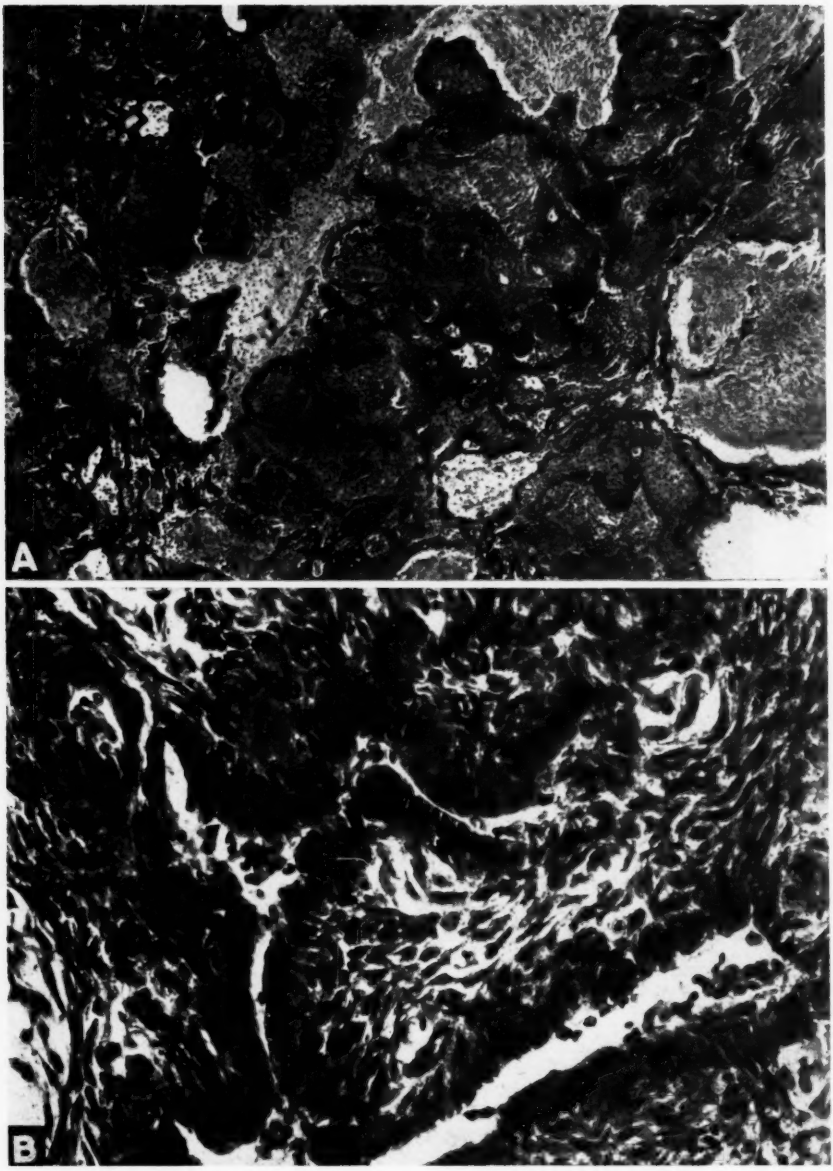


FIG. 3. (A) Low power view of the architecture of the tumor. (B) Detailed structure of an epithelial column. (Hematoxylin and eosin)

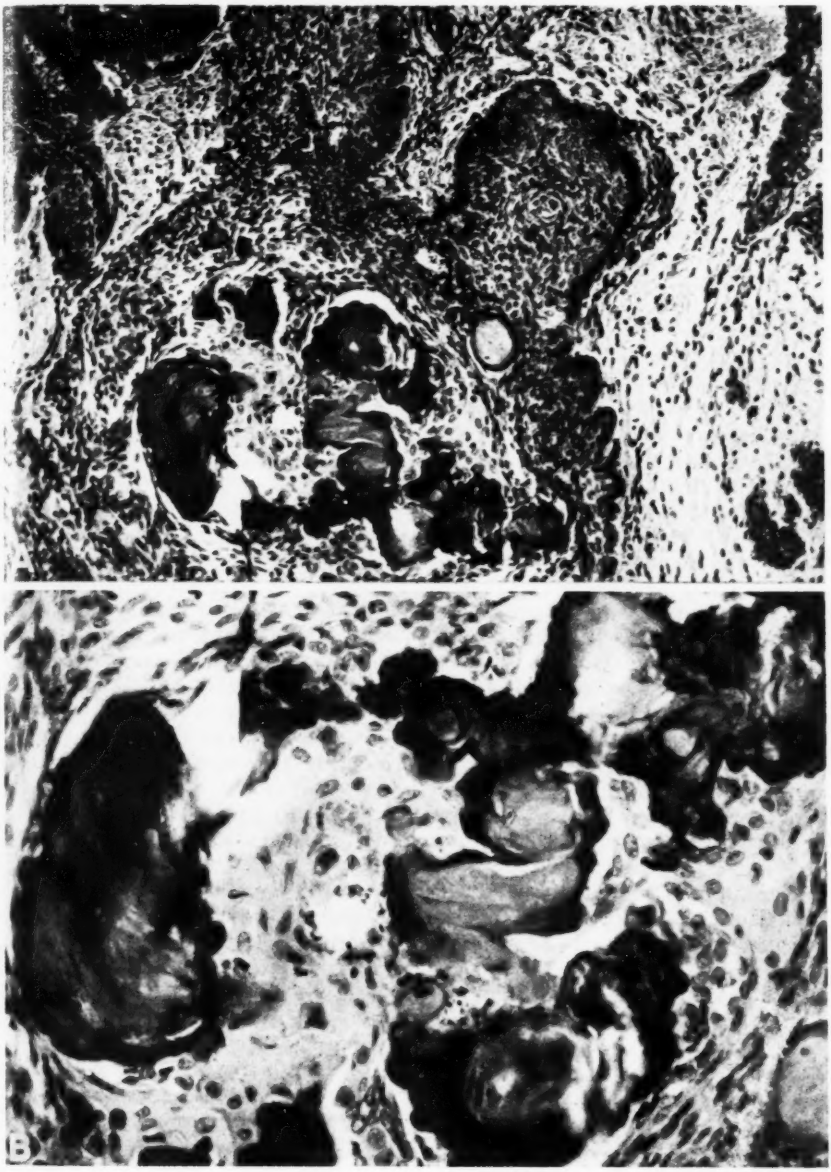


FIG. 4. (A) Medium power view of part of the tumor showing calcification in necrotic epithelium. (B) High power view of the calcific area depicted in (A). Note faint outlines of epithelial cells in the calcific masses. (Hematoxylin and eosin)

of blue-staining cytoplasm and dark oval nuclei. More centrally the cells were loosely arranged and were stellate or polygonal in shape. In the center of some of the columns keratinized cells and epithelial pearls were seen. Keratohyaline granules were not identified with certainty. There were numerous foci in which the epithelial cells were necrotic, and calcium deposits often occurred in these places (Fig. 4). Frank bone formation was not observed in the tumor but there were a few areas of osteoid tissue adjacent to the necrotic and calcific masses. Cysts were found in profusion; these either had walls of necrotic tumor tissue or were lined by flattened epithelial cells. The cysts usually contained blue-staining amorphous material, but in places angulated slits reminiscent of the presence of cholesterol crystals were found. The stroma of the tumor was abundant and consisted of fibrillar glia with a moderate admixture of collagenous connective tissue.

COMMENT

A remarkable variety of tumors occurs at the base of the skull in the vicinity of the pituitary body. Many of these are composed of cells foreign to the central nervous system and appear to arise from cells that have been displaced during fetal life. There is considerable movement of masses of cells from the roof of the buccal cavity and floor of the diencephalon in the formation of the pituitary body.[1,3] The upper part of the pouch of Rathke usually persists as a small narrow cleft between the anterior and intermediate lobes, to which its walls have given origin, and is lined by a single layer of columnar or cuboidal epithelium. The lower part of Rathke's pouch, often called the hypophyseal duct, is gradually obliterated and its epithelial lining is converted into a cord of cells or several islands of squamous epithelium along with the rest of the epithelium of the buccal cavity.[11] With the great increase in size of the anterior lobe, the pituitary body is rotated so that the attachment of the hypophyseal duct is carried upwards and forwards to the anterior surface of the infundibulum.[10] Islands of squamous epithelial cells are often found here in later life.[5] Glandular tissue and other dermal elements may in this way be carried into the cranial cavity where they are not naturally found and persist as "fetal rests" and "fetal displacements." These may on occasion give rise to tumors of several types. All are alike in being circumscript, noninvasive collections of abnormal cells. Although arbitrary criteria have been adopted for their identification there is still much confusion because of loose terminology. Some writers[9] applied the term craniopharyngioma to all tumors derived from Rathke's pouch whether cystic or solid, others[10] distinguish cysts arising from the terminal part of Rathke's pouch from tumors arising from epithelial rests along the obliterated hypophyseal duct. Cholesterol-laden adamantinomas are sometimes confused with epidermoids or cholesteatomas. There is, however, a general agreement among pathologists that the adamantinomas of the pituitary are benign epithelial neoplasms composed of multiple interlacing cords and columns of cells in a fibrous stroma. The epithelial columns have a peripheral layer of tall columnar cells closely set in palisade formation; the central stellate or polygonal cells are arranged in loose formation. The presence of the peripheral layer of columnar cells which resembles the ameloblast layer of the primitive tooth germ is the essential diagnostic feature of these tumors.[7]

Cysts of Rathke's pouch are essentially distension cysts of the cleft that remains between the anterior and intermediate lobes of the hypophysis. Grossly these present themselves as small usually intrasellar cysts containing chocolate-colored material. Microscopically they are seen to be lined by a single layer of cuboidal or columnar epithelium not infrequently ciliated.[13] Occasionally they may contain glandular structures in their walls and goblet cells.[10]

The epidermoids or cholesteatomas take origin from epithelial rests that are displaced into the cranium during the closure of the neural tube and the formation of the flexures of the primitive brain.[6] When they occur in the vicinity of the pituitary body they are, unlike the adamantinomas, usually located on one or the other side of the midline. These tumors have a characteristic opaque glistening capsule like the interior of a sea-shell. Microscopically the wall shows four concentric layers of different thickness.[2] The stratum granulosum is the essential diagnostic feature of these tumors and consists of several layers of oval or polygonal cells with clear intercellular spaces and intercellular bridges. The cytoplasm of these cells contains granules of keratohyalin which Love *et al.*[15,16] consider essential for diagnosis. The interior of the tumor grossly presents a pale yellow to white flaky lamellated appearance and microscopically consists of desquamated epithelium and cholesterol crystals. Dermoids are often of similar appearance but contain in addition derivatives from the corium, particularly hair follicles and sebaceous and sweat glands.

The gross and microscopic features of the tumor found in the infant reported above conform to the commonly accepted criteria for pituitary adamantinoma. The areas of keratinization of squamous cells, foci of epithelial necrosis with calcification, islands of osteoid tissue, and numerous cysts have all been described in previously published cases of pituitary adamantinoma.[7,12,16] The preponderantly glial stroma in this case is unusual; however a similar finding was recorded by Critchley and Ironside[7] in one of their cases. The relative avascularity of these tumors has been commented upon by Love *et al.*,[16] who ascribe the frequent degenerative changes in the tumor to this inadequacy of blood supply.

The enormous size of the tumor in the present case is not unusual. In the series of Frazier and Alpers[12] all the patients who came to necropsy had tumors extending from the optic chiasm to the anterior border of the pons. In their Case 8 in particular there was an enormous tumor that reached from the middle of the orbital surfaces of the frontal lobes to the anterior border of the pons. Likewise the pituitary bodies in all the cases that came to necropsy were not found, apparently having been compressed and atrophied beyond recognition by the tumor.

The remarkable degree of hydrocephalus and enlargement of the head that were the presenting clinical features was undoubtedly the result of the obstruction of the aqueduct by the tumor growing in the tegmentum of the midbrain. The expansion of the brain was not restricted by bony union of the vault of the skull. The absence of papilledema is of course the usual finding in hydrocephalus occurring before the fusion of the cranial bones.

Mention may be made of the inconstant findings on roentgenography of the head. It is surprising that there was no roentgenological evidence of calcification in the present case, for the tumor on section showed numerous calcium deposits. Whether these were dense enough to have produced shadows in a roentgenogram is a question that cannot be answered with certainty. It may be recalled, however, that not all adamantinomas show calcific shadows on roentgenography. Although McKenzie and Sosman[17] reported radio-opaque calcification in 71 per cent of cases in their series, Beckmann and Kubie[4] found only 4 instances in a series of 21 cases, and Frazier and Alpers[12] 7 in a group of 14 cases.

Adamantinomas of the pituitary have been reported to be more common in the adolescent and pre-adolescent years of life in contrast to the pituitary adenomas that occur in later years. Out of 92 cases of craniopharyngiomas that were mentioned

by Cushing,[9] slightly less than half occurred in patients under 20 years of age, and in the series of Frazier and Alpers,[12] 9 out of the 14 patients were under 20 years of age. The report of Peet[18] concerned 3 children all under 10 years; likewise the craniopharyngiomas of Ingraham and Scott[14] were all in children. The youngest reported patient to date was one of Cushing,[9] a child aged 3½ years; another mentioned by Ingraham and Scott[14] was aged 4 years. It is therefore believed that the patient in the present case is not only the youngest that has been reported but that the radiographic evidence of hydrocephalus in utero and its great size indicate that it must have arisen during fetal life. It is interesting to note that Cushing[8] had expressed his belief that these tumors develop before birth even though they manifest themselves clinically later. The case reported here would be the first to substantiate this hypothesis.

SUMMARY

A case is reported of a pituitary adamantinoma that was found in an infant 3 months old.

The tumor had led to massive hydrocephalus in fetal life.

It is a pleasure to acknowledge the valuable advice of Dr. R. D. Adams, lately visiting neurologist and neuropathologist, Boston City Hospital, and at present chief of neurology, Massachusetts General Hospital, Boston, in the preparation of this report.

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LUMBAR DISC PROTRUSION

A USEFUL SIGN

DONALD MCEACHERN, M.D.*

Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute, Montreal, Canada

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There is a sign of lumbar disc protrusion that often goes unrecognized. This was described some years ago but it was buried.[1] It consists of referred hyperalgesia and muscle spasm over back and loin when the appropriate area is stimulated.

The sign is of particular help in cases of low back pain or sciatica when localizing tests and the myelogram are negative. It has given us courage to explore the L4–L5 and L5-S1 intervertebral spaces in several cases. Operation revealed large disc protrusions, and removal gave immediate relief. These patients would otherwise have been doomed to incessant pain. Many patients with lumbar disc protrusion do not show this sign, but others do.

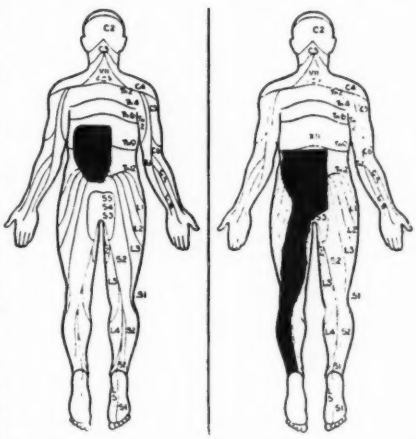

FIG. 1. Two examples of hyperalgesia associated with ruptured discs.

The Sign. The skin over the back on the affected side is very sensitive to the prick or stroke of a pin or to rough tactile stimulation. The sensation is described as "spreading," "vibrating," or painful; always as unpleasant and unusual. In this respect it resembles "thalamic" overresponse. The responsive area usually extends from the lower costal margin to the iliac crest behind, and occasionally down on to the buttock or even on to the sacral area on the back of the thigh and leg. On the loin, it extends forward only to about the posterior axillary line and does not involve corresponding segmental areas on the anterior abdominal wall. It is therefore not segmental in distribution.

Strong reflex contraction of the posterior spinal or intercostal muscles of the affected side may accompany stimulation of the skin, even when the stimulus is insufficient to cause unpleasant sensation. Two examples of the distribution of hyperalgesia are pictured in Fig. 1.

The phenomenon seems to be a referred hyperalgesia and is not due to root involvement. It disappears at once after operation. A possible explanation may lie in the intersegmental nerve supply of the dura and ligamentous structures.

The most recent case in which this evidence has proved of value is described below.

M.N.I. 51-7925. Mrs. I.C., aged 35, was admitted on May 17, 1951. She complained of low back pain dating from a fall on the buttocks in November, 1950. Recurrent episodes of severe back pain and bilateral sciatica took place in the interim. Prolonged bed rest and many types of physiotherapy failed to improve things except temporarily. She had come to be looked upon by physicians and friends as a confirmed neurotic.

* Deceased October 31, 1951.

Upon admission there were the usual signs of paraspinal muscle spasm and right-sided sciatica. She had lost 30 lbs. in weight. She was sleepless and harassed and could not look after her three children. No selective weakness, reflex, or sensory change could be made out in the lower limbs. Roentgenograms and a pantopaque myelogram of the lumbosacral region were negative.

Exquisite hyperalgesia was found, however, over the skin of the right loin, associated with brisk contraction of underlying muscles. This encouraged Dr. Arthur R. Elvidge to explore, and he did a bilateral removal of a large, soft and obviously diseased disc at the L4–L5 level.

Relief of pain was immediate, and the hyperalgesia had vanished by the following day. Four months later the patient was doing all her housework, was free of pain, and had gained 24 lbs.

SUMMARY

A helpful sign occurs in some cases of lower lumbar disc protrusion. When localizing tests and myelography give no clue, the sign may lead to successful surgical exploration and removal of the offending disc. It consists of hyperalgesia and reflex muscle contraction upon stimulation of the loin on the affected side. A description is given of the phenomenon.

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A SELF-RETAINING SPINAL DURA RETRACTOR

Ralph B. Cloward, M.D.*
Honolulu, Hawaii

(Received for publication September 7, 1951)

Prior to the article of Mixter and Barr in 1934[7] on the syndrome of the ruptured intervertebral disc, surgical attack upon spinal lesions anterior to the dural sac was seldom attempted. This was primarily due to the fear of the serious postoperative complication of hemorrhage. The first operations described for removal of a herniated intervertebral disc were performed by the transdural approach.[4] Extradural lesions above the cauda equina lying on the anterior wall of the spinal canal were usually attacked through the anterior dura or were often considered inoperable because of the danger of injury to the spinal cord by retraction and postoperative hemorrhage. The treatment was frequently only a spinal decompression.

With recent development of more efficient methods of hemostasis, including the improved electrical coagulation instruments, fibrin foam and gelatin foam with thrombin, the horizons of neurosurgery have been extended considerably. The extradural approach for ruptured intervertebral discs has been routine for the past ten years. Lesions such as tuberculous abscesses and granulomas, as well as tumors and cysts, and even large arthritic spurs situated anterior to the dural sac, at almost any level are now readily attacked by the extradural approach.

However, the surgery of this region, i.e., the anterior wall of the spinal canal, is still fraught with technical difficulties. The chief difficulty is the exposure of the lesion by retraction. Various methods of obtaining greater exposure have been used, namely the removal of a considerable amount of bone from the lateral wall of the spinal canal (including the vertebral pedicles and ribs), section of spinal nerve roots

* 388 Young Hotel Building, Honolulu 9, Hawaii.

and aspiration of spinal fluid from the dural sac. The instrument most frequently used to obtain an exposure of this region is a narrow nerve retractor or spatula. The surgeon's left hand must be relegated to the job of holding this retractor throughout the operation. The removal of the lesion, including dissection, traction, hemostasis, etc., must be done with one hand. If the use of a chisel is required, the surgeon must call upon an assistant to either hold the retractor or use the hammer, both of which are awkward and unsatisfactory. Few surgeons will place the responsibility of the instrument used for retraction of the spinal nerve roots, dura or spinal cord in the hands of an assistant.

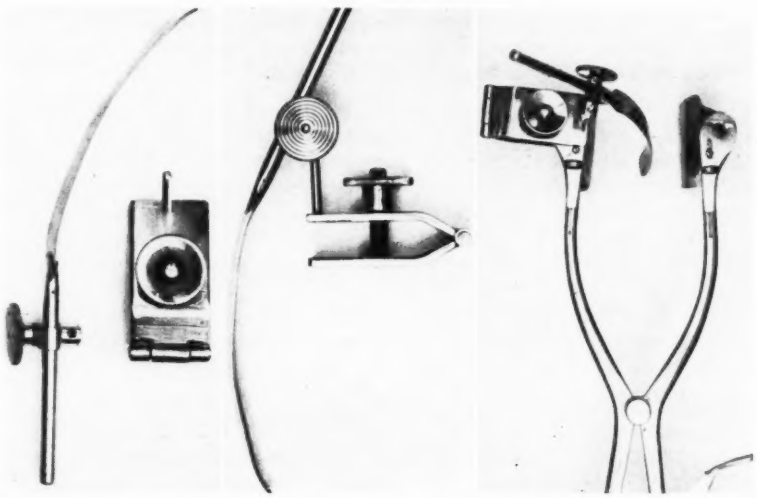

FIG. 1. The self-retaining spinal dura retractor is attached to a modified Hoen laminectomy retractor by a large hinged clamp. The spatula is placed beneath the nerve root or cord, secured and held firmly in place by the swivel-screw-clamp.

In 1943 the author began experimenting with an operation for the treatment of ruptured intervertebral discs. It consisted of removing a part of the disc through a hemilaminectomy exposure and replacing it with a large bone graft for the purpose of fusing the vertebral bodies.[3] This operation was gradually improved upon until it has now reached what is considered by the author to be the point of near perfection. The operation at the present time is done by a subtotal removal of the lumbar disc, including the cortex of the vertebral bodies. Three or more full-thickness bone grafts obtained from the iliac crest are driven into the intervertebral space through a partial bilateral laminectomy.

This procedure of fusing the vertebral bodies through the spinal canal has for many years been described by orthopedic surgeons as being too hazardous to be practicable, while admitting that it is the most logical and physiological method of spinal fusion.[2] The hazard of such an operation has been removed by the development of an instrument which the writer chooses to call a self-retaining spinal dura retractor.*

* This instrument is manufactured by Codman & Shurtleff Inc., 104 Brookline Avenue, Boston 15, Massachusetts.

The instrument consists of a simple hinged clamp which can be opened by twisting a fairly large knurled nut and fitted over the shaft of any self-retaining laminectomy retractor at a point where the blades are attached (Fig. 1). The clamp is secured tightly by twisting the large nut. On the incision side of the clamp is a vertical post, 3½ cm. high, to which is attached a screw-swivel-clamp having two holes. The vertical post of the clamp is passed through one hole and the handle of the retracting dural spatula through the other. The spatula blades are made in various widths. They have a convex curve at the tip to prevent pressure on the nerve or spinal cord by the edge of the spatula and are made of fairly stiff, but malleable metal so that they can be bent and shaped for the particular situation. The upper (round) end of the spatula is placed in the hole of the screw clamp and adjusted to the desired position and the screw is tightened. The spatula then remains in position until moved. This leaves the surgeon with both hands free to do the operation. The danger of injury to the nerve root, and/or the spinal cord which may occur from the constant pulling and hauling of these important structures with a hand retractor is minimized if not eliminated.

The ease with which surgery anterior to the spinal dura, particularly intervertebral disc operations, can be done with this instrument is most surprising. It has made the operation for fusion of the vertebral bodies a relatively simple procedure rather than a formidable one.[1] The danger of missing fragments of herniated intervertebral discs, as in the simple disc operation, is eliminated because there is a much greater exposure of the anterior dural space.[6] Finally, large midline disc protrusions and arthritic spurs in the cervical region compressing the spinal cord may be removed much more safely (by the transdural approach as recommended by D'Errico[5]). After cutting the dentate ligaments, the spinal cord may be retracted and held steady and stationary by the instrument, leaving the surgeon with both hands free to attack the lesion.

SUMMARY AND CONCLUSIONS

1. A new instrument, a self-retaining retractor for the spinal cord, dura and spinal nerve roots, is presented.

2. Its uses in the surgery of lesions lying anterior to the spinal dura, permitting the surgeon to use both hands instead of one to remove such lesions, are described.

3. It is predicted that this instrument will not only facilitate the operations described, but will reduce if not eliminate the not infrequent complications that are caused by injury from manual retraction of the spinal cord and nerve roots.

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NOTICES

AMERICAN ELECTROENCEPHALOGRAPHIC SOCIETY

The 6th annual meeting of the American Electroencephalographic Society will be held at the Hotel Claridge, Atlantic City, New Jersey, May 10 and 11, 1952. The scientific meetings will be held on Saturday afternoon and evening. On Sunday morning there will be a symposium on the electroencephalogram in relation to psychiatry. Dr. Denis Hill of Maudsley Hospital, London will participate in the symposium as a guest of the Society. Dr. Hudson Hoagland will be Chairman.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

At the 31st annual meeting of the Association for Research in Nervous and Mental Disease held in New York City on December 14–15, 1951, the following officers were elected for the year 1952: President, Dr. H. Houston Merritt; First Vice-President, Dr. Robert F. Loeb; Second Vice-President, Dr. Charles D. Aring; Secretary-Treasurer, Dr. Clarence C. Hare; Assistant Secretary, Dr. Rollo J. Masselink.

Two additional Trustees were elected to enlarge the Board of Trustees from five to seven. The new Trustees are Dr. H. Houston Merritt and Dr. Clarence C. Hare.

The subject for the 1952 meeting will be "Metabolic and Toxic Diseases of the Nervous System."

CANADIAN NEUROLOGICAL SOCIETY

The 4th annual meeting of the Canadian Neurological Society will be held at the Banff Springs Hotel, Banff, Alta., on June 8 and 9, 1952. The scientific sessions are open to non-members. Members of the Harvey Cushing Society are cordially invited to attend.

To leave Victoria on Saturday afternoon, June 7, and reach Banff Sunday morning, June 8, can only be done by catching the mid afternoon T.C.A. plane from Victoria to Calgary and then a train or bus from Calgary to Banff on Saturday afternoon or evening.

Sunday morning neurological papers will be given. Dr. F. M. R. Walshe will give a critical review of some neurological investigative methods. On Sunday afternoon there will be a Panel Discussion of some special aspect of vascular disorders.

On Monday morning Dr. Macdonald Critchley will give a paper on parietal lobe symptomatology. Monday afternoon will be devoted to a Symposium on "The Cerebral Cortex of Primates and Man," to which Doctors Walshe, Penfield and others will contribute.

Visitors will be welcome to attend the special attractions in Banff, and a Ladies' program is being arranged. All accommodations are being arranged by the Canadian Medical Association, which has taken both Banff Springs Hotel and Chateau Lake Louise for the week of June 8 to 13. The scientific sessions of their annual meeting will be held June 10 to 13.

Requests for hotel reservations for the Canadian Neurological Society meeting should be made as soon as possible to Dr. A. E. Wilson, 904 Grey Hound Building, Calgary, Alberta. These applications for accommodation, when possible, should be made in the form as printed in the Canadian Medical Association Journal, Nov. 1951, p. 496; Dec. 1951, p. 607.

THE NATIONAL PARAPLEGIA FOUNDATION

The National Paraplegia Foundation wishes to announce the continuation of a limited number of fellowships for research in spinal cord disease and trauma and in the complications associated with such disease or injury. These fellowships carry a minimum stipend of $3000 per year and may be awarded to any candidate who has demonstrated a capacity for medical research and has outlined a program of meritorious study. The fellowships will be awarded by the Medical Advisory Committee and are open for award for the academic year 1952–1953. Application forms may be obtained from Dr. L. W. Freeman, Chairman, Medical Advisory Committee, Indiana University School of Medicine, Indianapolis, and should be submitted to him not later than May 1, 1952.

THE NEW YORK SOCIETY OF NEUROSURGERY

Dr. Gilbert Horrax, neurosurgeon to the Lahey Clinic, to the New England Deaconess Hospital and to the New England Baptist Hospital, Boston, will deliver the annual Charles A. Elsberg Lecture, established by the New York Society of Neurosurgery, on March 18, 1952 at the New York Academy of Medicine, at 8:30 P.M. His subject will be: "The Development of Brain Tumor Surgery."

CEREBRAL ANGIOGRAPHY IN CHILDREN

AN ANATOMOCLINICAL EVALUATION

JORGE A. PICAZA, M.D., M.S.

Neurosurgical Department, Hospital Municipal de Infancia, Havana, Cuba

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During the last few years numerous papers pertaining to cerebral angiography have been written. Most of the authors included cases of angiography in children, but usually the number has been small and proper evaluation of how children tolerate the procedure as well as its usefulness in this age group has not been presented. We have thought it worthwhile to analyze a series of 50 cases of different conditions in children verified by necropsy or operation, in which cerebral angiography has been carried out as an adjunct to neurologic diagnosis.

TECHNIQUE

In the great majority of the cases in this series angiography was performed by direct exposure and injection of the common carotid artery in the neck (open technique). In only 7 cases was puncture of the vessel made directly through the skin (percutaneous technique). A short transverse incision, 2 or 3 cm. long, at the level of the cricoid cartilage, is enough to expose the vessel after a brief dissection with scissors. Barbiturates and local infiltration with novocain provide a good anesthesia in patients within the first 2 years of life, but general anesthesia, using ethyl chloride and open drop ether, had to be given in most of the remaining cases to secure adequate immobilization during the radiographic exposures. Infants have a short neck making the procedure more difficult, but in the later ages children with long and skinny necks are most suitable for the percutaneous technique if cooperation can be secured.

COMPLICATIONS

The following complications were encountered:

Convulsions	3 cases
Pneumomediastinum	2 cases
Bernard-Horner syndrome	3 cases

Convulsions appeared during the test in 3 cases. All 3 patients had had convulsions for some time before angiography was performed. One was suffering from encephalitis, 1 from focal epilepsy and 1 from subarachnoid hemorrhage. Two of them were injected with a 75 per cent solution of the contrast medium, the use of which was subsequently discontinued, being replaced by a 35 per cent solution. The convulsions were Jacksonian or tonic and generalized, disappearing spontaneously in a few minutes following the injection.

There were 3 patients who showed a cervical sympathetic paralysis which disappeared within a period of 8 weeks. All these patients were operated upon by the open technique and probably the sympathetic chain was damaged during the dissection of the carotid artery in the neck. In 2 cases there was moderate polypnea with subcutaneous crepitation in the neck during 24 to 48 hours following the procedure. Roentgenograms of the chest revealed a pneumomediastinum that cleared up spontaneously without consequence. Following the injection some patients complained of soreness of the neck for 24 to 48 hours and were relieved by ice bags.

Usually the injection was done on the side where the lesion was suspected, but bilateral and multiple injections (as many as five), using 50 cc. of 35 per cent solution, have been repeated without any apparent disturbance. We have used as contrast media Diodrast (Winthrop), Neo Iopax (Shering) and Pyelectan (Glaxo), with little difference in results and complications, as long as the solution was not higher than 35 per cent concentration. We did not see such complications as thrombosis, embolus, recurrent laryngeal palsy, hematoma and sensitivity reactions, described by previous authors in cases of adults, all the complications herein studied being benign and reversible.

ANATOMOCLINICAL STUDY

Angiography was performed 66 times in a series of 50 children ranging from 9 days to 15 years in age. These patients were affected by various neurological conditions in which it was thought that an angiographic study might be of some help in the diagnosis. In 23 cases the vascular pattern was found to be abnormal, providing important information about the character of the disease in most instances (Table 1).

TABLE 1

Results of angiography in children

Final Diagnosis	No. of Cases Studied	Pathologic Angiograms
Brain tumor	12	8
Hydrocephalus not due to brain tumor	3	3
Cerebral malformations	8	8
Acrocephalosyndactylism	1	1
Vascular disease	5	3
Others*	21	0
Totals	50	23

* Including encephalitis, diffuse and focal atrophy, subarachnoid hemorrhage, toxoplasmosis (?) meningovascular lues, and orbital tumor (3 cases).

BRAIN TUMORS

Of the 12 cases of brain tumor studied, 4 failed to show any pathologic change of the cerebral vessels: 2 brain-stem gliomas, 1 craniopharyngioma

and 1 cystic astrocytoma of the cerebellum. The carotid as well as the vertebral artery was injected in the cases of the posterior fossa lesions. On the other hand, 5 tumors of the cerebral hemisphere were shown definitely by the arteriograms. Astrocytomas and hemangioblastomas, either cystic or solid, appeared as avascular areas spreading away the arteries in the cortex (Figs. 1, 2 and 3). Glioblastomas pushed the vessels away but there was in-

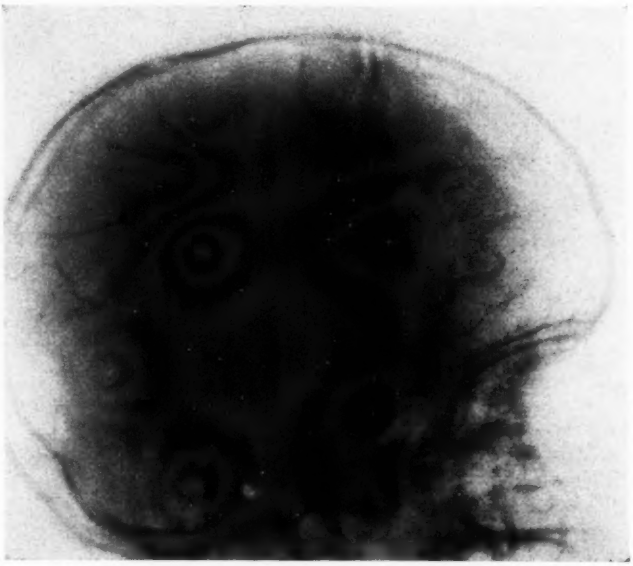


FIG. 1. E.P., a 12-year-old boy. Increased intracranial pressure and left facial weakness. Percutaneous arteriogram. The middle cerebral artery is pushed upwards. Cystic astrocytoma of right temporal lobe.

creased vascularity in the cortex in the area where the tumor extended to the surface of the hemisphere, with enlarged veins forming a corona. These tumors sometimes show neoformations of small vessels within the substance of the neoplasm itself. In this respect our findings agree with those obtained in adults by List and Hodges,[2] Green and Arana,[1] and others (Fig. 4). In 3 cases of orbital tumors (epidermoid, hemangioma and fibrosarcoma) the angiograms showed no appreciable pathologic change of the vessels. Angiography seems to be particularly important in the etiological diagnosis of a focal cerebral lesion, for an expansive lesion can sometimes be discovered in a very early stage (Fig. 2).

HYDROCEPHALUS

Although the clinical diagnosis of hydrocephalus may be obvious in infants, due to the enlargement of the head, in later ages this disorder is sometimes mistaken for a chronic expansive intracranial lesion. However, the

FIG. 2. O.H., a 7-year-old girl. Slight headache and difficulty in writing for a month. Increased reflexes and right facial weakness. No signs of pressure. Left parietal focus in EEG. Left parietal solid subcortical astrocytoma.

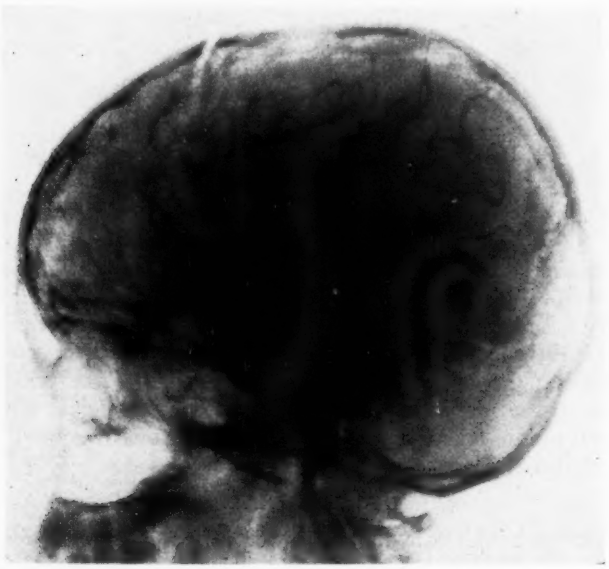


FIG. 3. J.C. Recurrent convulsions 4 years followed by increased pressure Cystic hemangioblastoma of left temporoparietal area.

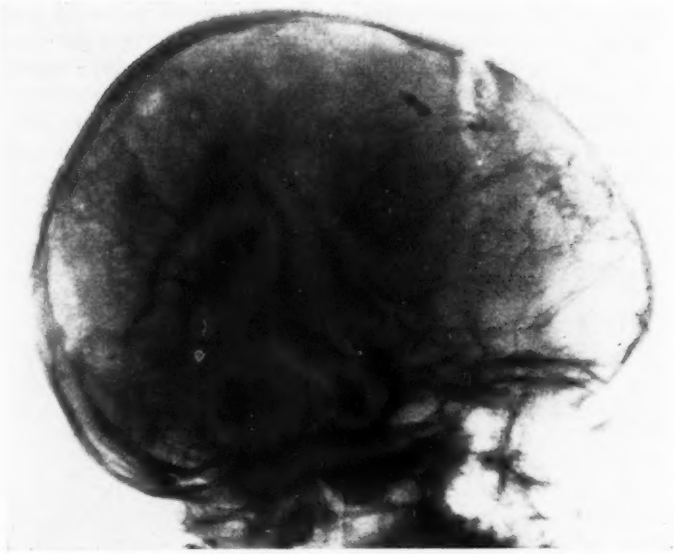


FIG. 4. F.A. Progressive symptoms of increased pressure with amblyopia. Combined angiogram and ventriculogram. Right frontal glioblastoma.

FIF. 5. Combined venticulogram and arteriogram in hydrocephalus. Typical appearance of the arteries in an advanced case.

differential diagnosis may be aided by angiography. Internal hydrocephalu is easily recognized by characteristic alterations in the vascular pattern, es pecially as shown in the arteriogram. In the lateral view the usually shar bend of the middle cerebral artery is changed into a broad curve, the vesse running in a diagonal course. On the other hand, the anterior cerebral artery makes a wider curve surrounding the corpus callosum (Fig. 5). Though these findings are typical of internal hydrocephalus, they give no information a to its cause and usually further studies should be carried out in order to ar rive at a definite diagnosis.

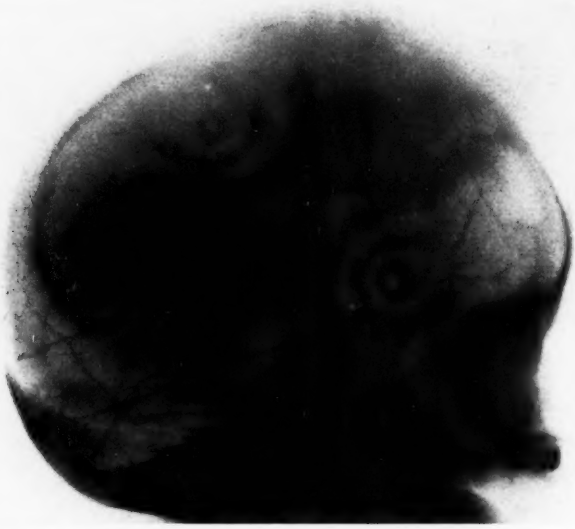


FIG. 6. Hydroencephalodysplasia. Note the hypoplastic internal carotid artery and absence of collateral branches from middle cerebral artery.

MALFORMATIONS

There are a certain number of infants who show an enlargement of the head and increased intracranial pressure but who are not suffering from the usual internal hydrocephalus. They are affected by an extensive cerebra dysplasia and a collection of fluid under pressure. We have called this mal formation hydroencephalodysplasia.* The differentiation between interna hydrocephalus and hydroencephalodysplasia should be established since the malformation has a poor prognosis and is not suitable for surgery.

In congenital internal hydrocephalus, angiography reveals elongated ar teries in the characteristic arrangement described above. On the other hand in hydroencephalodysplasia the internal carotid artery is small and hypo

* To be published.

plastic, and its branches are abnormal, incomplete or absent. The Sylvian group has been seen to be formed by only two arteries running parallel to one another, without branches (Fig. 6). The internal carotid artery may end abruptly in a small bunch of fine vessels. The middle cerebral artery has been shown without any of the ascending branches to the cortex (Figs. 7 and 8). The abnormality of the vessels changes from one case to another, depending on the amount of cerebral tissue that is absent. In contrast, the external carotid artery and branches are well developed in all cases.

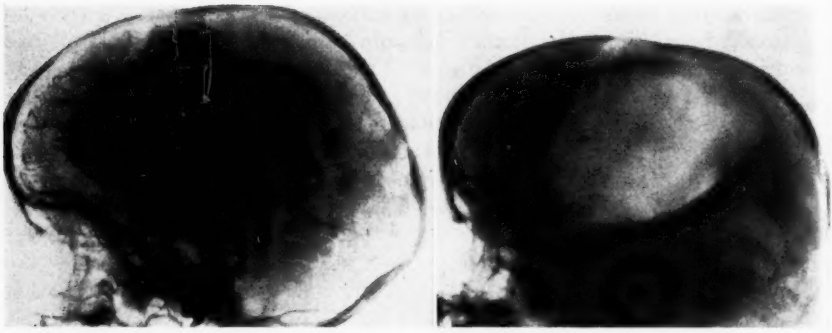
Figs. 7 and 8. H.E.D. Hydroencephalodysplasia. (*Left*) Absence of frontoparietal branches from middle cerebral artery. (*Right*) Ventriculogram showing agenesis of frontoparietal area.

Clinically this malformation can be suspected whenever a child with an enlarged head shows signs of optic atrophy, arrested development, or spasticity. Unfortunately before the 4th or 5th month of age these symptoms are not easily recognized. Subdural punctures yielding fluid in great amounts make the diagnosis quite possible but angiography gives a typical picture.

Porencephaly is another malformation that can be revealed by arteriography. As in other dysplasias, the diagnosis is based on the absence of a number of cerebral arteries. It is a requisite of correct diagnosis that the remaining arteries be well filled, otherwise artefacts in technique with filling defects could be misleading. There is also no complementary collateral circulation as occurs in thrombosis. It is possible that not all porencephalic cysts can be diagnosed by angiography since it is known that a number of them are covered by a thin layer of nervous tissue crossed by vessels (Figs. 9 and 10).

BLOOD-VESSEL DISEASE

Angiography shows its most beautiful results in the diagnosis of blood-vessel lesions, particularly malformations and aneurysms. The clinical symptoms of these lesions in children are scanty and the disease therefore is frequently not kept in mind by the general practitioner and probably goes



FIGS. 9 and 10. G.B., a 15-month-old boy. Recurrent convulsions followed by hemiplegia. (*Left*) Porencephalic cyst in parietomotor area. (*Right*) Pneumoencephalogram showing huge porencephalic cyst.

unrecognized among the often-seen cases of epilepsy, hemiplegia and cerebral hemorrhage of the early ages.

A spontaneous hemorrhage (intracerebral or subarachnoid) may be the only clinical expression of a vascular cerebral malformation (Fig. 11). The importance of its diagnosis is emphasized by the fact that localized lesions are nowadays amenable to surgery. Usually the case appears as one of chronic convulsions until a vessel ruptures and a spontaneous hemorrhage occurs. The only way of making an early diagnosis is by performing angiography in children with convulsions that show any evidence of a focal cerebral lesion (Fig. 12).

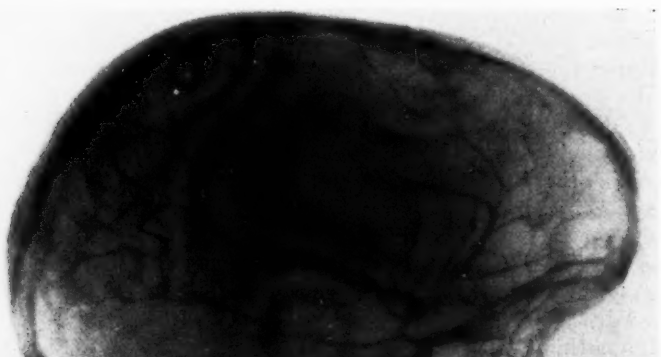


FIG. 11. A 15-year-old girl with spontaneous subarachnoid hemorrhage and right-sided hemiplegia with aphasia. Small arterial angioma in motor area.

FIG. 12. A 12-year-old boy with recurrent right Jacksonian attacks. Left parietal focus on EEG. Arteriovenous aneurysm in parietomotor area.

The existence of a peripheral angioma associated with neurological symptoms does not necessarily imply that a similar lesion will be revealed by cerebral angiography. In 2 cases of Sturge-Weber syndrome the angiograms failed to show abnormalities, and in a case of Parke-Weber congenital hemangiectasis, in which a huge angioma of the leg was well shown in angiograms of the affected extremity, the cerebral vessels were normal in spite of the fact that the patient suffered from convulsions. In another case, in which there were extensive arteriovenous malformations of the extracranial blood vessels, angiography failed to reveal intracranial abnormalities. Our material does not include studies of cerebral hemorrhage in the newborn; this deserves special consideration.

RESUME

The author analyzes and correlates the anatomoclinical and X-ray findings in 50 children on whom cerebral angiography was performed for neurologic purposes. The technique proved to be safe although not easy to perform in infants. The results were of value in the diagnosis of a number of supratentorial tumors, vascular malformations and hydrocephalus. The procedure has been used with success in discovering cases of cerebral malformation in infancy (porencephaly, hydroencephalodysplasia). Illustrative examples are presented.

RESUMEN

Los autores analizan y correlacionan las caracteristicas anatomo-clinicas

con los hallazgos radiologicos de cincuenta niños en los cuales se realizó l
angiografía cerebral, con fines de diagnostico. La técnica resultó segu
aunque no fácil en los lactantes. Resultó ser de valor en el diagnostico de l
tumores cerebrales supra-tentoriales, malformaciones vasculares ó hidr
cefalia interna. Tambien fué empleada con éxito en el diagnostico de l
malformaciones cerebrales que pueden ser vistas en la infancia (anencefali
porencefalia, hidroencefalodisplasia). Estas conclusiones son ilustradas co
ejemplos.

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EXTRADURAL HEMATOMAS OF THE POSTERIOR FOSSA

LLOYD J. LEMMEN, M.D., AND RICHARD C. SCHNEIDER, M.D.
Department of Surgery, Section of Neurosurgery, University of Michigan Medical School and Hospital, Ann Arbor, Michigan

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EXTRADURAL hematomas of the posterior fossa, which result from trauma, present variable clinical signs and symptoms. These lesions may present neurological signs that localize the abnormality to this region. More frequently they are seen in combination with concurrent lesions elsewhere resulting from the same trauma, and with a paucity of clinical findings their presence may not be recognized.

This report adds to the literature 3 cases, in 1 of which the lesion, as early as could be ascertained, was limited to the posterior fossa. The other 2 cases, with supratentorial hemorrhage, illustrate the wide variety of clinical signs and symptoms encountered with patients who also harbor an epidural hematoma of the posterior fossa.

REPORT OF CASES

*Case 1.** D.B., a 52-year-old, right-handed, white male prisoner at Southern Michigan Prison, was struck over the head three times with an iron pipe by another inmate at 2 P.M. on Aug. 21, 1951. Although severely dazed, he had no period of unconsciousness or retrograde amnesia. There was pronounced bleeding from the scalp laceration in the right posterior parietal area and profuse CSF otorrhea and hemorrhage from the right ear. Headache became progressively more severe and there were several bouts of vomiting.

Roentgenograms of the skull revealed a linear fracture through the occipital bone and through the right petrous ridge (Fig. 1). There was air in the subdural space along the falx (Fig. 2).

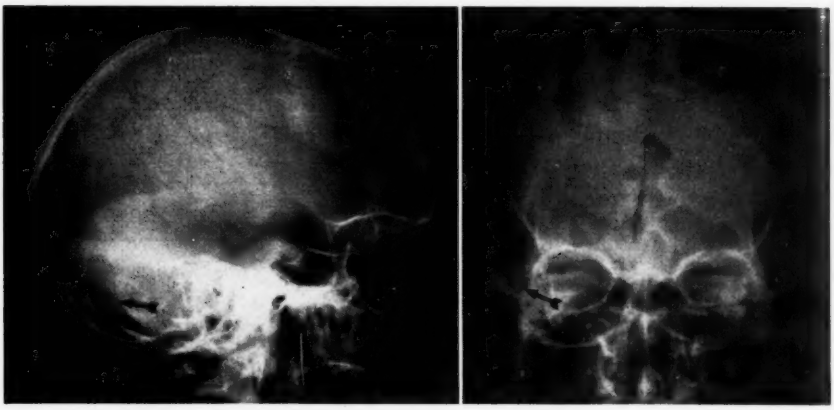
Course. The 8 cm. scalp laceration was debrided by Dr. James Fish who carefully observed the patient's vital signs. On Aug. 23, 1951, he was unable to speak as clearly as previously and Cheyne-Stokes respirations developed with rather prolonged periods of apnea.

Neurosurgical Consultation. B.P. 132/84, pulse rate 80, and respirations 22 (Cheyne-Stokes in character). There was a profuse right CSF otorrhea. The patient was alert and oriented. The pupils were equal and reacted to light and in accommodation. A rotatory and right horizontal nystagmus were present. The right ear was deaf. The speech was of bulbar type with paralysis of the right side of the palate. The right sternocleidomastoid and trapezius muscles were paretic. There was ataxia on finger-to-nose test, more marked on the right side. The patient was immediately prepared for operation.

Operation. Under intratracheal anesthesia, a trephine opening was made in the

* The authors wish to express their appreciation to Dr. Russell Finch, Medical Director, Southern Michigan Prison, Jackson, Michigan, for the privilege of presenting Case 1.

right occipital region just above the lateral sinus and another was made at right Keen's point (3 cm. above and 3 cm. behind the external auditory meatus). The dura was opened at these points. The underlying brain did not pulsate and did not extrude from the dural openings. No other abnormality was seen. An incision was then made in the right suboccipital area and a linear fracture line was found about 3 cm. above the foramen magnum. Upon unroofing this area, an extradural hematoma, approximately 2.5 cm. in thickness and 6 cm. in diameter, was observed extending slightly beyond the midline. No definite bleeding point could be identified and upon removal of the clot the dura pulsated freely. The trephine incisions in the supratentorial



FIGS. 1 and 2. *Case 1.* Roentgenograms of skull showing (*left*) linear fracture through the occipital bone and (*right*) fracture in right petrous ridge and air in subdural space along falx.

regions were closed and it was then noted that the dura in the right posterior fossa no longer pulsated as readily. Therefore, it was incised and a portion of destroyed right cerebellar hemisphere and intracerebellar clot extruded. A cortical vessel extending to the occipital sinus was thought to be the origin of the intradural hemorrhage. This was coagulated and in order to remove the devitalized tissue a quarter of the right cerebellar hemisphere had to be removed. The dura was left open and the wound closed tightly.

Course. The patient was placed on a regime of penicillin, streptomycin and sulfadiazine. Within 48 hours there was complete disappearance of the nystagmus, the 9th, 10th, and 11th cranial nerve palsies, and the finger-to-nose ataxia. For the first 5 days after operation the temperature ranged between 102° and 103° rectally, and during this period the right otorrhea continued. On the 6th day there was no further CSF drainage from the ear and the temperature dropped to normal. On the following day a right peripheral 7th nerve palsy appeared. Subsequently, there was a gradual clearing of this palsy and the patient has remained asymptomatic.

Comment This patient presented a typical extradural hematoma of the posterior fossa and this was thought to account for the major clinical signs and symptoms. Whether the dura should be opened, if one finds an extradural hematoma, depends upon the surgeon's evaluation of the variable factors in the individual case.

The presence of a cerebrospinal fluid otorrhea in a case of extradural hematoma involving the posterior fossa presents an additional complicating factor in the diagnosis of a clot. With the drainage of cerebrospinal fluid through the ear, the patient decompresses himself intracranially, thus minimizing the signs and symptoms of increasing intracranial pressure until the lesion has attained considerable size.

Case 2. E.O., a 14-year-old, right-handed boy, was admitted to University Hospital 6 days after a head injury. On July 31, 1951, while riding his bicycle, he was struck by a car traveling 50 miles an hour. He was unconscious for 24 hours, then gradually began to improve until he was able to recognize his mother 4 days after the accident. Following this he continued to be drowsy and had frontal headaches; these symptoms persisted until his entry to the hospital.

FIG. 3. *Case 2.* Photograph of patient showing ptosis of left eyelid, 6th nerve palsy on the right, and right central facial palsy.

FIG. 4. *Case 2.* Roentgenogram of skull showing separation of lambdoid suture on the left. →

Examination. B.P. 128/86, pulse rate 76, respirations 18, and temperature 100.4°. There were old abrasions over the left face and forehead. A large soft subgaleal hematoma was present over the left occipitoparietal area. There was a 6th nerve palsy on the right with an almost complete external ophthalmoplegia on the left. The left eyeball was in the primary position with little voluntary or following movement in any direction. A ptosis of the left lid was present. The pupils, however, were round and equal and reacted to light and in accommodation. No nystagmus was present. There was an early bilateral papilledema. Except for a right central facial palsy, the remainder of the cranial nerves were intact (Fig. 3). There was a mild right hemiparesis, more marked in the arm than in the leg. Finger-to-nose

testing and other coordinated movements were done less well on the right than on the left. Muscle tonus was decreased bilaterally and the patient was hyporeflexic. There were no sensory changes.

Lumbar puncture revealed a pressure of 700 mm. of water; the fluid was clear with a cell count of 4 lymphocytes.

Roentgenograms of the skull revealed a separation of the lambdoid suture on the left over the occipital lobe (Fig. 4). An open arteriogram was done on Aug. 7, 1941 which showed a displacement of the anterior cerebral artery to the right across the

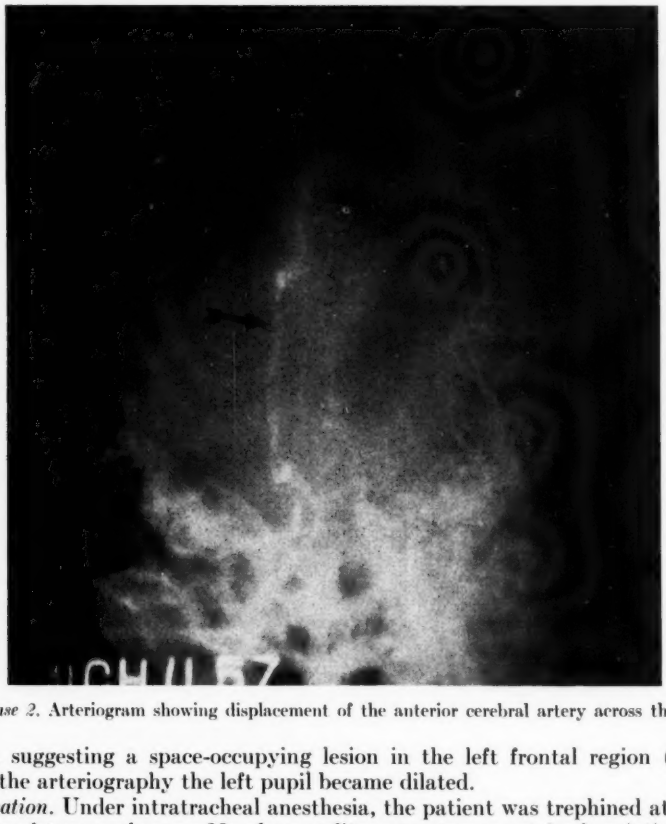


FIG. 5. *Case 2.* Arteriogram showing displacement of the anterior cerebral artery across the midline.

midline, suggesting a space-occupying lesion in the left frontal region (Fig. 5). During the arteriography the left pupil became dilated.

Operation. Under intratracheal anesthesia, the patient was trephined at the left coronal and temporal areas. No abnormality was seen except for herniation of the brain through small openings made in the dura. Trephination at Keen's point on the left disclosed an extradural hematoma, which depressed the dura 3 cm. from the skull and was composed of dark red blood which passed through the suction tubing with difficulty. A five-hole bone flap was made in the left occipitoparietal area and the clot was found to cover the left cerebral hemisphere behind the interaural plane. There was active bleeding from the separated lambdoidal sutures. By extradural retraction of the occipital pole, blood could be seen below the tentorium. Bleeding

was controlled with oxycel and gelfoam. A small dural opening revealed no abnormality. The dura was sutured to the overlying pericranium and the bone flap returned to its bed. Trephine and dural openings were made at the right coronal, temporal, and parietal regions and no abnormality was seen. A trephine was then made over the left posterior fossa and the opening enlarged. A hemorrhage, 1 cm. in thickness and 6 cm. in diameter, was found over the dura of the left cerebellar hemisphere. This was completely evacuated. Dural opening showed no further pathologic condition. A Penrose drain was left in the wound in the posterior fossa and was removed in 48 hours.

Course. The patient gradually began to clear mentally. Forty-eight hours after operation, the right pupil became dilated but continued to react to light. The eye movements gradually began to return, and during this period there was nystagmus on right lateral gaze with the quick component to the right. At the time of the patient's discharge from the hospital, Aug. 20, 1951, there was no longer any papilledema. A mild ptosis of the left eyelid persisted. Nystagmus was present on right lateral gaze. The 6th nerve weakness on the right had disappeared. There was a fairly good range of eye movement on the left with the best action looking downward. The right pupil was still larger than the left; however, both reacted to light and in accommodation. The patient was seen one month after operation and was found to have no neurological abnormality except for some residual paresis of the left lateral rectus muscle.

Comment. Anisocoria is seen infrequently in cases of extradural hematoma of the posterior fossa. In the reported cases[6,8,11] of patients who had pupillary abnormalities and who were operated upon, large lesions covering both occipital and posterior fossa regions were found. We do not know how to account for the ptosis, ophthalmoplegia and pupillary responses, but feel that they must be related to the clot because of the return of function after its evacuation. The late appearance of pupillary changes in these cases would suggest that the initial findings were not entirely on the basis of a temporal pressure cone.

Case 3. P.H., an 11-year-old, right-handed girl, was hit behind the left mastoid process by a baseball on Aug. 13, 1951. Following the accident she became lethargic and vomited several times. She was seen by her family physician who found a pulse rate of 40. While en route to University Hospital she had several episodes of disorientation. She was admitted 12 hours after injury.

Examination. B.P. 96/60, pulse rate 80, respirations 20, and temperature 98.6°. The patient was very lethargic, but cooperative. There was no aphasia. Pupils were round and equal and reacted to light and in accommodation. No other cranial nerve abnormality was demonstrable. The patient was unsteady in the erect position; the left side of the body was ataxic on coordinated movements, the arm more than the leg. No skin laceration or palpable hematoma was present.

Roentgenograms of the skull showed a depressed fracture of the occipital bone over the left transverse sinus (Fig. 6). A posterior fossa hematoma was immediately suspected.

While the operating room was being prepared, the right pupil began to dilate. She became more drowsy, complained of severe headache, and had several episodes of projectile vomiting.

Operation. Under intratracheal anesthesia, the fracture over the transverse sinus was exposed through an L-shaped incision over the left posterior fossa. The fracture was found to be depressed over the sinus and the fracture line extended into the mastoid process. The depressed bone was removed and the bony defect enlarged over the dura of the occipital lobe. Active bleeding was seen coming from the fracture lines extending into the mastoid process. An extradural hematoma, 2 cm. in thickness, was found over the left hemisphere behind the interaural plane. The clot was

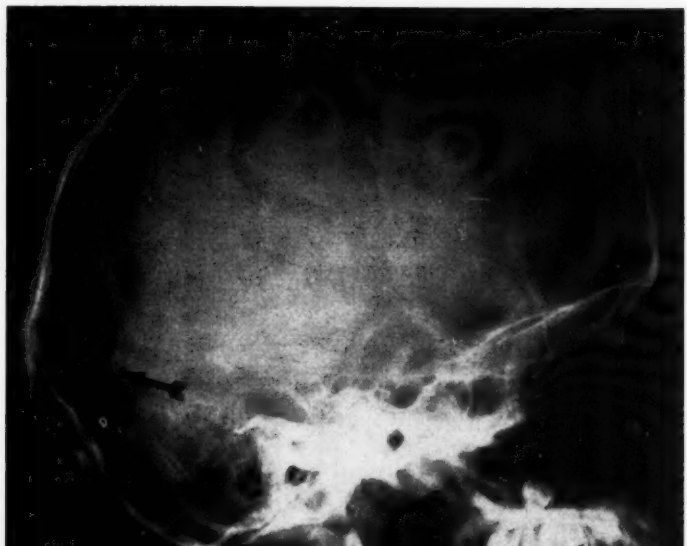


FIG. 6. *Case 3.* Roentgenogram of skull showing depressed fracture across the left transverse sinus

evacuated through the bony defect and through a trephine made over the left posterior parietal region. Trephine and dural openings at the left temporal and coronal areas showed no further hemorrhage. An extradural hematoma, 0.5 cm. in thickness and 5 cm. in diameter, was removed from the dura covering the left cerebellar hemisphere. All the clot was removed and the bleeding was controlled with oxycel and gelfoam. After the dura over the cerebellum was opened and no abnormality found, it was sutured to the overlying pericranium. A trephine at Keen's point on the right revealed no abnormality.

Course. The patient was discharged on the 8th postoperative day with no demonstrable neurological abnormality.

Comment. It would appear that extradural cerebellar clots may be formed acutely or may accumulate more slowly. The rapid accumulation of blood between the dura and skull presents the surgeon with a true eme-

gency. In Cases 1 and 2, the lesion in the posterior fossa was considerably larger than in Case 3, in which the lesion was seen much earlier after the trauma. It is very possible that the extradural hematoma over the posterior fossa in Case 3 by itself might not have been of surgical significance; however, in this instance there were clinical signs and symptoms of its presence.

DISCUSSION

Extradural hematoma of the posterior fossa is a rare clinical entity. In a study of several large series of head injuries, the lesions limited to the posterior fossa have an incidence of 0.5 per cent of all extradural hemorrhages.[14] Cases in which this lesion was found, operated upon, and clot successfully removed, have been reported by Anderson,[1] Bacon,[2] Coleman and Thomson,[3] Fleminger and Smith,[4] Kessell,[9] Meredith,[12] Schneider, Kahn, and Crosby,[14] Scoville,[15] Turnbull,[16] and Watts.[18] Operated cases of combined lesions of the posterior fossa and occipital region have been reported by Grant and Austin,[6] Gurdjian and Webster,[7] Herren and Zeller,[8] and McKenzie.[11] Additional cases of these types have been reported from autopsy material.[5,8,10,13,17]

Coleman and Thomson,[3] in presenting the first case of closed extradural cerebellar hematoma reported, suggest the following diagnostic criteria for such a lesion:

> There is a history of a blow on the back of the head severe enough to produce a fracture of the skull but which may or may not cause unconsciousness. This is followed by headache of gradual increasing severity and is usually accompanied by nausea and vomiting. Drowsiness and restlessness appear and progress until the patient lapses into unconsciousness. However, during the drowsy state several things may be noted. The patient prefers to lie on one side and will promptly return to the same side when placed upon his back. Nuchal rigidity develops, nystagmus may or may not be present, and the deep reflexes disappear. As unconsciousness deepens, generalized hypotonia develops, the pulse and respirations become irregular and death is imminent unless there is prompt surgical intervention with removal of the clot.

Nystagmus, hypotonia, hyporeflexia, cerebellar fits, and cranial nerve abnormality may be of great value in localizing this lesion, but too often these signs are masked by concurrent supratentorial lesions. In surveying the literature, there is no one definite clinical picture common to all. The single important factor in making the diagnosis of the extradural hematoma of the posterior fossa is the high index of suspicion that such a lesion may exist.

The treatment of extradural hematoma is prompt recognition of its presence, followed by trephination of the suspected area. Should a clot be uncovered, the incision can be enlarged and craniectomy carried out until the source of bleeding is identified and controlled. Further recurrence of this condition is prevented by retention sutures in the dura to the overlying pericranium.

The most common sources of bleeding in these lesions are the lateral

sinus and the torcular Herophili. Fractures through the foramen magnum and petrous ridge or separation of suture lines[1] may be responsible for the clot. In certain cases no fracture is demonstrable.[9,14,16] In many instances the presence of a contusion or laceration of the scalp may give suggestion of an underlying lesion.[5] Schneider, Kahn, and Crosby[14] suggested that if the presence of an occipital fracture extending downward through the foramen magnum and contusion or laceration of the scalp is observed in a patient who has remained unconscious or is becoming more comatose, and in whom the state of unconsciousness cannot be attributed to a supratentorial lesion, there is sufficient evidence to warrant trephination over the posterior fossa. This concept should be enlarged to include a spreading of the lambdoidal sutures and fracture lines that traverse the lateral sinus.

In cases where the more anterior portions of the skull are trephined for possible middle meningeal bleeding, trephination may give little indication of an extradural bleeding in the more posterior portions of the skull, and its presence may not be recognized if multiple trephines are not made. McKenzie[11] has emphasized that in cases where an occipital lobe extradural hematoma is discovered at trephination, another trephine should be made in the suboccipital region to rule out an extension into the posterior fossa. The same is true if the clot is found initially in the posterior fossa.

The prognosis in extradural hematoma of the posterior fossa is favorable if the condition is recognized early. The reported cases in the literature indicate that these patients have an excellent chance of recovery if prompt evacuation of the extradural clot is performed.[8] This is true in our series of 4 cases (including the case previously reported by Schneider, Kahn, and Crosby[14]) in which we have removed an extradural cerebellar clot, since all the patients have made complete recoveries and are well.

SUMMARY

1. Three cases of extradural hematoma involving the posterior fossa have been reported showing a variable clinical picture.

2. In the presence of supratentorial lesions, the presence of the extradural lesion in the posterior fossa may not be recognized because of a paucity of clinical findings.

3. Intracranial decompression by cerebrospinal fluid otorrhea may minimize the signs of increasing intracranial pressure so that the presence of an epidural hematoma of the posterior fossa may not be recognized.

4. Early recognition of this condition, followed by evacuation of the extradural clot, offers the patient an excellent chance of complete recovery

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A COMPARISON OF POLYETHYLENE AND TANTALUM FOR CRANIOPLASTY

A PRELIMINARY REPORT

CAPTAIN WALTER S. LOCKHART, JR., M.C., U.S.A., LIEUT. GORDON VAN DEN NOORT, M.C., U.S.A., MAJOR WARREN H. KIMSEY, M.C., U.S.A., AND ROBERT A. GROFF, M.D.*

Neurosurgical Section, Surgical Service, Valley Forge Army Hospital, Phoenixville, Pennsylvania

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ANIMAL experimentation in 1947 by Ingraham, Alexander and Matson[5] with polyethylene in contact with the brain and its coverings showed the plastic to be innocuous to the tissue studied.

Busch[2] reported in 1949 the successful use of polyethylene plate for cranioplasty in 8 patients.

Alexander and Dillard[1] used polyethylene for cranioplasty and in 1950 described its advantages over other materials, citing experimental and clinical data from their own investigations and reviewing the literature concerning the properties of polyethylene and the tissue-response to this material. Polyethylene cranioplasty was reported in 5 patients. The report emphasized that polyethylene is firm, resilient, radiolucent, easy to fashion at the operating table and innocuous to tissues. Its cost is about 1/50 that of tantalum.

As is widely known, tantalum has been used successfully during recent years in large numbers of cranioplasties.[3,4,6,7]

The present study is of the immediate results of cranioplasty in a group of 24 patients with skull defects following war injuries. Polyethylene was used in 12 patients. Tantalum was used in an equal number of patients. The same operating team performed surgery on both groups.

CLINICAL MATERIAL

All 24 patients were overseas casualties from the Korean Area. Twenty-two had open craniocerebral missile injuries. Two had closed head injuries with depressed skull fractures. All had had craniectomies at overseas hospitals.

Operative notes made at overseas hospitals indicated that in instances in which the dura was not penetrated by the missile, opening of the dura was carried out to determine if subdural hematoma was present.

Removal of reasonably accessible bone fragments and metallic foreign bodies had been accomplished overseas.

As a result of preparation at overseas hospitals, the edges of the skull

* Associate Professor of Neurosurgery, Graduate School of Medicine, University of Pennsylvania, Philadelphia.

defects were universally rather smooth and dural defects, where present, had been covered with galeal, epicranial or fascia lata grafts. The average skull defect was 6 cm. in diameter. This study did not include cranioplasty over a previously injured frontal sinus or repair of any supraorbital skull defects.

Five of the patients had had major infections with cerebral abscess or infection in the scalp flap. None had had osteomyelitis of the skull.

In the cases where cerebral abscess or infection in the scalp flap had been present, the average length of time between injury and cranioplasty was 10 months. In those cases where there had not been infection, the average length of time between injury and cranioplasty was 6 months.

All patients had been ambulatory for at least 4 months and were without exception well-nourished young adults in good general physical condition.

OPERATIVE METHODS

Polyethylene. The polyethylene plate,* 3 mm. in thickness, was sterilized by scrubbing for 10 minutes with soap (Septisol) followed by immersion for 24 hours in 1:1,000 aqueous Zephiran solution.

The cranial defect was exposed and the pericranium incised circumferentially 1 cm. from its margin. The pericranium was then resected centrally together with any excessive scar tissue overlying the dura. A ledge then was formed in the bone edge by using a hammer and gouge, or dental drill with burr, to remove the outer table of the skull to a width of 1 cm. about the entire circumference of the defect (Fig. 1).

FIG. 1. A prepared skull defect showing the shelf at its edge before insertion of a polyethylene plate.

A rough pattern of the defect was prepared with cloth, x-ray film or aluminum foil. The polyethylene plate was fashioned roughly from this pattern by using tin shears, or a linoleum-cutting knife, and the desired contour was obtained by manual molding during immersion in hot water.

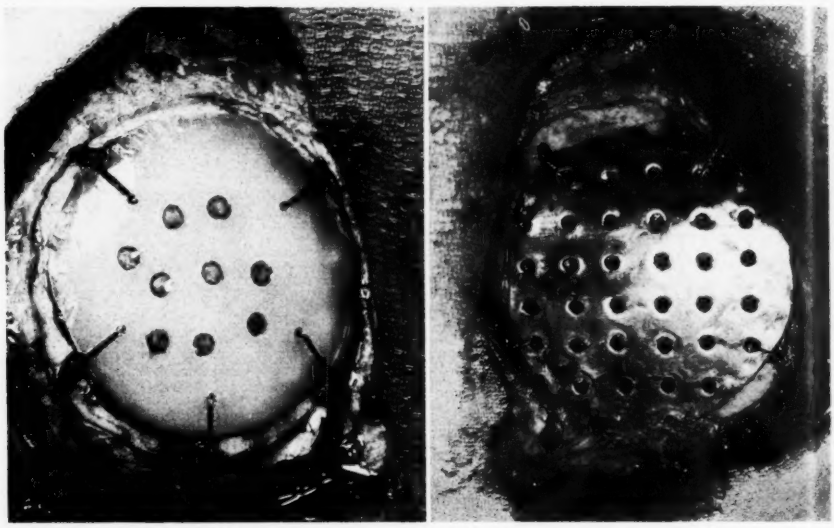
When the desired contour was obtained, it was set by immersing the plate in cold water for 1 minute. The edges of the plate then were shaved and beveled with a linoleum-cutting knife and scalpel to obtain a smooth, tight fit in the defect with the surface of the plate flush with the outer surface of the skull.

Multiple perforations, approximately 5 mm. in diameter, to permit the escape of any accumulation of fluid or blood under the plate, were drilled in the polyethylene. These perforations also permit granulation tissue to protrude and ultimately be-

* Obtained from Plastics Department, du Pont de Nemours & Co. (Inc.), Arlington, New Jersey.

come scar tissue. It is expected that the plate thus will become more firmly secured following the initial stabilization with No. 2 silk passed through small drill-holes at the edge of the defect and at the edge of the plate (Fig. 2).

Tantalum. A perforated tantalum plate, 0.015-inch thick, was cut to size, following a cloth pattern obtained from the skull defect. This was hammered into shape on a skull-shaped anvil of bronze. When laid over the defect, with an overlap of about 0.5 cm. beyond the edge of the defect, it was held in place with 0.018-inch stainless steel wire which linked the perforations with drill-holes at the edge of the defect. The ends of the wire were twisted and inserted into the drill-holes (Fig. 3).



FIGS. 2 and 3. (*Left*) Perforated polyethylene plate secured in place with No. 2 silk. (*Right*) Tantalum plate secured in place with 0.018-inch stainless steel wire.

GENERAL ROUTINES

General anesthesia with endotracheal intubation was used for all but 2 patients who had local procaine anesthesia.

When very thin temporal bone was found at an edge of a defect, tantalum was chosen because of difficulties in countersinking polyethylene in such instances.

Penicillin was given postoperatively for 10–15 days. Dilantin and phenobarbital were given prophylactically after operation for about 3 weeks.

All patients were allowed to be ambulatory on the 1st or 2nd postoperative day.

Patients were observed for an average period of 4 months following cranioplasty.

RESULTS

The average operating time for polyethylene and tantalum was approximately the same.

All wounds healed without infection. X-rays after operation showed no osteomyelitis. A moderate amount of subgaleal fluid accumulated in 3 patients after tantalum cranioplasty and in no patient after polyethylene cranioplasty. This minor complication was transient, and aspiration of the scalp was not carried out in any case.

One tantalum plate was removed because of the development of headache and status epilepticus within 3 weeks after cranioplasty. Subsequent observation of this patient indicated that he had a severe personality disturbance and had volitional control of his seizures.

No other patient developed headache after cranioplasty. Headache, when present before operation, was not significantly altered after cranioplasty. Likewise, visual disturbance, speech difficulty, convulsive seizures, weakness of the extremities and intellectual impairment—when present before operation—were unchanged after operation.

Moderate intolerance to exposure to hot sun was offered as a complaint by 8 patients with tantalum plates. No patient with a polyethylene plate had this complaint.

SUMMARY

1. Polyethylene was used for cranioplasty in 12 patients and tantalum in an equal number. The results are compared.

2. Preliminary evaluation of the patients studied indicated confirmation of the previously described qualities of polyethylene as a substance useful in cranioplasty.

3. The advantage of being able to tolerate exposure to hot sun was emphasized by the patients with polyethylene plates.

4. Tantalum was selected when thin bone edges were encountered because of the difficulty in countersinking polyethylene in such instances.

5. One tantalum plate had to be removed because of headache and seizures after cranioplasty. Causal relationship between operation and the complication is questionable.

6. Moderate subgaleal fluid accumulation occurred after tantalum cranioplasty in 3 instances and after polyethylene in no instance.

7. Otherwise, both substances were well tolerated without complication.

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CLINICAL COMPLICATIONS OF CEREBRAL ANGIOGRAPHY

KENNETH H. ABBOTT, M.D.,* JAMES R. GAY, M.D., AND ROBERT J. GOODALL, M.D.

Columbus, Ohio

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THE purpose of this paper is to summarize the untoward effects of cerebral angiography as we have encountered them clinically in 150 patients upon whom we have performed 174 cerebral angiograms. We wish further to emphasize the several factors or mechanisms that may be etiologic in the development of these complications. This report is not intended in any way to condemn the use of cerebral angiography for we feel that it is one of the greatest advances in our means for the diagnosis of intracranial lesions since the introduction of pneumoencephalography and ventriculography by Dandy.

With the present extensive use of cerebral angiography as an aid in the diagnosis of many different intracranial neurologic problems, there is a need for an adequate evaluation of the coincidental reactions and complications of this very valuable diagnostic procedure. Although there are many reports in the literature concerning various complications that have arisen consequent to cerebral angiography, it would appear that there is a need again to emphasize that cerebral angiography may not be as innocuous a procedure as some have indicated. Our experience has shown, and we wish to herein emphasize, there can be no doubt that not a few of these complications are a matter of ill-advised or poorly executed techniques employed, while other untoward manifestations may be assigned to the contrast media, and finally a few of these must always be inherent dangers in doing cerebral angiography.

In our series of 150 cases in which angiography was performed there were 32 tumors, 25 aneurysms, 13 subarachnoid hemorrhages (no aneurysm found), 3 subdural hematomas, 4 intracerebral hematomas, 14 cerebral thromboses, 3 with thrombosis of the internal carotid artery,† 17 cerebral degenerative syndromes (arteriosclerosis, atrophy, etc.), 1 meningovascular syphilis, and 38 miscellaneous (8 normal vascular patterns and a heterogeneous group of cases).

In this group serious untoward complications were encountered in 17 cases with 5 fatalities. In 2 instances less serious though alarming signs were noted.‡ The following case reports detail these major complications. Other less serious and transitory complications will be discussed.

* 350 East Broad Street, Columbus 15, Ohio.

† One with thrombosis of one internal carotid artery and thrombosis of the contralateral middle cerebral artery.

‡ Since this was submitted for publication we have performed over 100 more percutaneous cerebral angiograms, observing the precautions herein outlined, and in only 1 instance were there even transitory neurologic complications.

REPORT OF CASES

1. FATAL CASES

(A) *Delayed onset of unconsciousness, respiratory failure and subsequent death occurring with a normal cerebrovascular system.*

Case 1. An angiogram was done because of fixed pupils and bilateral facial and orbital pain of undetermined etiology with negative pneumoencephalogram in a 38-year-old white female. After failure in finding the right common carotid artery by the percutaneous technique, the open method was used. In this case only the right carotid artery was exposed. A total of 40 cc. of 35 per cent diodrast was employed. Because of restlessness and difficulties in the x-ray technique 5 cc. of 2½ per cent pentothal were given intravenously and two 5 cc. injections of 70 per cent diodrast were made into the right carotid artery. Excellent roentgenograms were obtained in the AP and lateral views. The patient awakened immediately after this complaining of a severe pain in her eyes, an accentuation of one of her chief complaints. There were no other untoward complaints or neurologic sequellae, until an hour and 20 minutes after the last angiogram was taken when central respiratory failure suddenly developed, and 2 hours later complete respiratory failure ensued. In spite of the aid of a respirator, stellate ganglion procaine blocks, serum albumin, plasma, lumbar punctures, metrazol and caffeine, death occurred. Postmortem examination confirmed the clinical evidence of cerebral edema with additional pathologic findings: 1) Bilateral gasserian ganglionitis, chronic, severe; 2) marked cerebral edema with pressure cone formation at the foramen magnum; 3) persistent thymus and relatively large lymph nodes; 4) hypoplasia of the breasts and mild hirsutism; 5) probable mild platybasia. (A review of the roentgenograms revealed a grade I platybasia.)

Delayed (30 minutes) loss of consciousness, sudden respiratory failure and death occurring in 2 cases of atherosclerosis and thrombosis of the internal carotid with cerebral infarction.

Case 2. A 53-year-old white male was studied because of progressive left hemiparesis. Difficulties were encountered in doing carotid angiography by the percutaneous method and therefore the open method was used. It was recognized that the right carotid appeared firmer than usual but the needle was inserted into it anyway. Blood flowed only fairly well and although it was suspected that it might be thrombosed, 10 cc. of 35 per cent diodrast were injected into the carotid. The angiograms disclosed a "blotch" of dye, measuring $5 \times 2\frac{1}{2}$ cm. in its greatest diameter, in the region of the distribution of the middle cerebral artery. This was thought to be a diffusion of the diodrast into the infarcted area. There was only a thin streak of dye seen in the thrombosed internal carotid artery. Central respiratory failure occurred about 30 minutes after the last diodrast injection followed in a few minutes by cardiac arrest. At subsequent examination there was found an infarction of the major portion of the right hemisphere with obvious thrombosis of the right common and internal carotid arteries and with healed ancient coronary thrombosis and myocardial fibrosis.

Case 3. A 38-year-old white male was hospitalized because of right hemiplegia and total aphasia. This came on approximately a week after severe hemorrhage from a duodenal ulcer. Bilateral cerebral angiography was done under pentothal anesthesia, using 60 cc. (!) of 35 per cent diodrast on each side. He failed to regain consciousness and died 12 hours later. Autopsy disclosed an atherosclerotic plaque in

the left internal carotid artery with thrombosis extending into the left middle cerebral artery and consequent severe infarction of the major portion of the left cerebral hemisphere. In addition there was unusually severe cerebral edema with punctate hemorrhages in the brain stem. (Fatality due to angiography?)

(B) *Immediate convulsions, subarachnoid hemorrhage (from ruptured aneurysm) during diodrast angiography, and subsequent death.*

Case 4. A white female, aged 39, was hospitalized on Dec. 19, 1949, 12 days following a severe subarachnoid hemorrhage with right hemiplegia and a complete left 3rd nerve palsy. On Dec. 21 a retrograde right carotid diodrast injection was made to visualize the vertebral-basilar-posterior cerebral artery system (it erroneously had been assumed that the patient had a Weber's syndrome). On each of three injections of 10 cc. each of 70 per cent diodrast the patient became unconscious with labored respirations. The eyes rolled up and there was spontaneous nystagmus to the right. She recovered consciousness in the matter of a few seconds each time. Following this, 10 cc. of 35 per cent diodrast were injected into the right internal carotid to make lateral views of the cerebral circulation with compression of the contralateral carotid. However, there was inadequate visualization of the left cerebral vessels. On Jan. 5, 1950, after she had shown marked improvement, another attempt was made to find the left vertebral artery, but without success. This time 50 per cent diodrast was used in the right carotid artery, again using the retrograde carotid technique. The patient had an immediate generalized convulsion and failed to regain consciousness. A lumbar puncture was done immediately while she was still on the x-ray table, revealing a very bloody spinal fluid. She died in a respirator 18 hours later. Autopsy disclosed a large aneurysm attached to the anterior origin of the left posterior communicating artery which had ruptured.

(C) *Subarachnoid hemorrhage, recovery, followed by angiography producing transitory hemiplegia and delayed recurrent subarachnoid hemorrhage and death.*

Case 5. A 47-year-old man entered the hospital in a semicomatose condition with a bloody spinal fluid. His condition gradually improved until he became conscious and cooperative. However, slight mental confusion and slight right-sided pyramidal tract signs persisted. Two weeks later left carotid angiography was carried out by the percutaneous method. Immediately after the third injection of 15 cc. of 35 per cent diodrast a right hemiplegia and total aphasia occurred. The procedure was then terminated and the patient was returned to his room, but before doing so the left stellate ganglion was blocked with 1 per cent procaine. Histamine diphosphate, 2.75 mg. in 250 cc. of 5 per cent glucose and water, was given by continuous slow intravenous drip. Within 10 minutes after starting the histamine his speech returned and there was almost complete recovery of function in the right extremities, at least to the point of being as good as it was prior to the episode. Later on in the day the patient had another episode of severe headache and unconsciousness due to a recurrence of the subarachnoid hemorrhage, and he died within 24 hours. The cerebral angiograms suggested that there was an aneurysm posteriorly in the circle of Willis that is, at the junction of the posterior cerebral and posterior communicating artery. (Might not this death have been due to the use of vasodilators?)

II. NON-FATAL COMPLICATIONS (PERMANENT)

(A) *Precipitation of hemiplegia by angiography.*

Case 6. A 39-year-old white man was seen in July, 1950 because of right frontal headaches of sudden onset with nausea and vomiting and subsequent development of ptosis of the right upper lid. Right carotid percutaneous angiography was carried out under pentothal sodium anesthesia without any difficulty, using a total of 30 cc. of 35 per cent diodrast. Approximately 6 hours after angiography he was still comatose and by this time there was an evident left hemiplegia (which was suspected immediately after the last injection of diodrast). The right Horner's syndrome was still present. The CSF was clear and the pressure was 140 mm. of fluid. He was treated with right stellate ganglion procaine blocks and intravenous histamine but though he recovered from the comatose state after 18 hours there was no improvement in the hemiplegia. It was evident that cerebral thrombosis had taken place in this case, the cause of which may have been the presence of an atheromatous plaque in the internal carotid artery or the middle cerebral artery.

Case 7. A 63-year-old physician underwent cerebral angiography because of rather rapid mental deterioration and neurologic signs suggesting the presence of a left frontal lobe lesion. Under light intravenous sodium pentothal anesthesia left carotid percutaneous angiography was done using 15 cc. of 35 per cent diodrast at each injection. After the third injection the patient suddenly displayed a right hemiplegia with deep coma. The angiograms disclosed a pattern consistent with that of a left frontal lobe astrocytoma. Craniotomy with amputation of the anterior half of the left frontal lobe was then done immediately. The tumor proved to be a grade II astrocytoma. The coma and right hemiplegia persisted after surgery, although later he did begin to move the right extremities a very little. He died 12 days after surgery. Autopsy was not permitted.

(B) *Accentuation of pre-existing hemiplegia with associated cerebral symptoms (aphasia, motor, sensory or both; and total aphasia, homonymous hemianopsia, anosognosia of Babinski, etc.)*

Case 8. A 53-year-old white man had experienced a slowly progressive left hemiparesis and left homonymous hemianopsia with astereognosis in the left hand. Right carotid angiography was carried out by the percutaneous method under 1 per cent procaine local infiltration anesthesia. About 20 cc. of 35 per cent diodrast were sufficient to obtain good cerebral angiograms. The patient immediately experienced marked increase in the weakness of the left extremities to the point of hemiplegia. The angiograms were indicative of a glioblastoma multiforme in the right parieto-occipital area. Craniotomy with subtotal removal of the tumor was done immediately. (The hemiparesis gradually receded following surgery but later became complete.) However, he succumbed 2 months later from extension of the tumor.

Case 9. Cerebral angiography was done on this 67-year-old man because of frequent transitory episodes of fronto-orbital headaches, tinnitus, giddiness, hypesthesia and slight weakness in the left side of the face. Examination disclosed arteriosclerotic retinal vessels as well as generalized arteriosclerosis. There was a suggestion of weakness of the lower left facial muscles and very slight hypesthesia over the left half of the face, and positive left Babinski and Mayer signs. The right carotid angiogram (open technique, using a total of 30 cc. of 35 per cent diodrast) failed to dis-

close more than arteriosclerotic cerebral vessels. Untoward symptoms following angiography consisted of marked increase in the motor and sensory deficit in the left face and upper extremity with coincident pyramidal tract signs. These symptoms gradually receded, disappearing on the third day. Later a pneumoencephalogram disclosed multiple areas of cerebral atrophy, suggestive of cerebral arteriosclerosis with multiple small old vascular occlusions.*

III. NON-FATAL COMPLICATIONS (TRANSITORY)

(A) *Hemiplegia.*

Case 10. This 44-year-old man was seen because of marked loss of vision with chronic, low-grade papilledema, irregular and constricted visual fields with severe hemianopsia and central scotoma in the left eye. In the right eye there was evidence of an old optic neuritis with superimposed papilledema. An opticochiasmatic arachnoiditis was the considered diagnosis but the presence of a neoplasm in this region could not be ruled out. Left carotid angiography (open method) was performed under local anesthesia with 35 per cent diodrast, using a total of 75 cc. Following injection of the last 15 cc. the patient immediately became unconscious for a few minutes and manifested a right hemiplegia. Upon regaining consciousness a severe right motor and sensory aphasia was apparent, with subsequent improvement. Repeated examination disclosed right homonymous hemianopsia (thus adding to the severe loss of vision he already had) and a typical visual-verbal agnosia. The sensory aphasia gradually disappeared with persistence of the motor aphasia and right hemiparesis for a period of 3 days, whereupon on awakening on that morning all of his symptoms had disappeared. He was treated with stellate ganglion procaine blocks, continuous intravenous drip of histamine, pyribenzamine, lumbar punctures, and transfusion of serum albumin and of whole blood. A few days later craniotomy disclosed extensive adhesions (arachnoidal) about the optic chiasm and optic nerves. Microscopic study of the arachnoid about the chiasm revealed a typical proliferative arachnoiditis. He has had no further difficulty and his visual fields have improved.

Case 11. This 45-year-old white man was studied for severe, early morning headaches and a single grand mal seizure. Following right percutaneous carotid angiography (local anesthesia, procaine), using a total of about 50 cc. of 35 per cent diodrast, a left hemiplegia developed which lasted for 48 hours with complete recovery. The angiograms failed to reveal any pathologic condition.

Case 12. A 50-year-old white woman was investigated angiographically for headaches and uncinate fits. She was most uncooperative, requiring repeated diodrast injections several times. (Therefore the angiograms should have been done under general anesthesia.) The "open method" was chosen, using the right common carotid artery. A total of about 100 cc. of 35 per cent diodrast was used. A left hemiplegia developed immediately following the injection of the last 15 cc. of the contrast medium. The hemiplegia lasted 2½ days followed by complete recovery. The cerebral lesion proved to be a glioblastoma multiforme.

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* We had another similar experience in a 47-year-old woman. In this case percutaneous carotid angiography was performed, using approximately 30 cc. of 35 per cent diodrast. There was evidence of arteriosclerosis with "minor vascular episodes." Hemiplegia developed immediately following angiography and disappeared in 3 days. So far we have not had this happen again except once when using thorotrast.

(B) *Precipitation of a transitory hemiparesis with other associated neurologic symptoms.*

Case 13. A 24-year-old student was admitted to the University Hospital because of a spontaneous subarachnoid hemorrhage. Two and a half weeks later bilateral exposure of the common carotid arteries (open technique) and bilateral cerebral angiography were done under local procaine anesthesia. A total of 60 cc. of 70 per cent diodrast was used by multiple injections (10 cc. each) for anteroposterior and right and left lateral views. The carotid angiograms disclosed a normal vascular pattern. There were no immediate complaints but after the patient reached his room it was noted that there was a mild left hemiparesis and rather marked left homonymous hemianopsia. The hemiparesis increased in intensity over a period of 6 hours accompanied by the homonymous hemianopsia and gradually receded over a period of 3 days. He made a complete recovery.

Case 14. A 70-year-old woman complained of progressive loss of vision to the point of almost complete blindness in one eye and complete temporal loss of vision in the other. It was thought she might have a suprasellar cyst. Angiography (open technique) was carried out under local procaine anesthesia, using a total of 24 cc. of thorotrast. There were no difficulties during the procedure, but immediately afterwards she displayed moderate mental confusion and complained of awkwardness in the use of the left extremities. Within a few hours there was definite left hemiparesis of mild intensity with marked mental confusion. These symptoms all cleared up in a period of 36 hours with the aid of multiple right stellate ganglion procaine blocks and intermittent intravenous etamon therapy. The patient proved to have a suprasellar cyst (craniopharyngioma) which subsequently was partially extirpated without complications. One year later she was doing well, but after 14 months signs of hypothalamic failure developed and she died after 16 months.

Case 15. A 47-year-old man of Jewish descent was studied because of right Jacksonian seizures. Left common carotid angiography (open technique) was done under local procaine anesthesia, using a total of 50 cc. of 35 per cent diodrast. For a period of 6 hours immediately following the last injection there was slight right hemiparesis with positive Babinski and confirmatory signs. All signs and symptoms disappeared by the end of this 6-hour period. A pneumoencephalogram showed a generalized enlargement of the ventricles and subarachnoid spaces suggestive of cerebral atrophy.

Case 16. A 48-year-old negro woman was referred for study because of progressive bitemporal hemianopsia to the point of almost complete loss of vision in one eye and complete temporal visual loss extending into the nasal field in the other eye. Lateral roentgenograms of the skull suggested the presence of a tuberculum sellae meningioma. Right percutaneous carotid angiography was done using a total of 55 cc. of 35 per cent thorotrast. Within a few minutes it was evident that she had a motor aphasia and left motor and sensory hemiparesis with delusion of body scheme (anosognosia of Babinski). These symptoms were severe for about 30 minutes and then gradually receded over the succeeding 2 hours with complete recovery. At operation the tuberculum sellae meningioma was found to be unusually large, completely enveloping both optic nerves and the chiasm.

(C) *Cerebellar fits (transitory decerebrate state) with immediate recovery.*

Case 17. A 53-year-old woman was seen because of a spontaneous subarachnoid hemorrhage. Approximately 3 weeks following this, when she had shown marked

improvement in her general status, cerebral angiography (open technique) was carried out, using the right internal carotid artery. A normal pattern was seen in the anterior and middle cerebral artery distributions. We therefore chose to do Elvidge and Ecker's (modified from Moniz, 1933) retrograde right carotid injection method of visualizing the vertebral and basilar arteries. Twelve cc. of 70 per cent diodrast were then used at each of two injections. With each injection the patient became unconscious and rigid, displaying a rather typical decerebrate state. This lasted between 1 and 2 minutes, with return to full consciousness. There were no residual symptoms. The angiogram revealed a large aneurysm of the basilar artery. These symptoms did not occur on visualization of the right cerebral vessels with 35 per cent diodrast.*

SUMMARY OF CLINICAL SYMPTOMS IN OUR SERIES OF INTRACRANIAL COMPLICATIONS OF CEREBRAL ANGIOGRAPHY

A review of our material reveals that the intracranial complications of cerebral angiography may be divided from a symptomatological standpoint into the following groups: I. *Fatal complications:* (A) Sudden onset of unconsciousness, respiratory failure and subsequent death occurring (1) with a normal cerebrovascular system and (2) in atherosclerosis and thrombosis of the internal carotid and cerebral infarction. (B) Immediate convulsions, subarachnoid hemorrhage (from ruptured aneurysm) during diodrast angiography and subsequent death. (C) After a subarachnoid hemorrhage, angiography producing transitory hemiplegia, followed by recurrent subarachnoid hemorrhage and death. II. *Non-fatal complications* (*permanent*): (A) Hemiplegia (precipitation of). (B) Accentuation of pre-existing hemiplegia with associated cerebral symptoms (aphasia, motor, sensory or both, and total aphasia, homonymous hemianopsia, anosognosia of Babinski, etc.). III. *Non-fatal complications* (*transitory*): (A) Hemiplegia (motor, sensory or both). (B) Hemiparesis (motor, sensory or both), and associated with these have been total aphasia, motor aphasia (various types), sensory aphasia (amnesic, auditory verbal agnosia, visual verbal agnosia, color agnosia, color aphasia, delusion of body scheme, acalculia, revisualization and recall defects), homonymous hemianopsia and mental confusion. (C) Cerebellar fits (transitory decerebrate state) with immediate recovery (in 2 patients with vertebral angiography with diodrast). (D) Minor fever (up to 102.6°) with or without transitory mental confusion.

The extracranial complications we have encountered may be summarized as follows: (1) Cervical hematoma necessitating tracheotomy (pericarotid and peritracheal hemorrhage). (2) Severe irritation of cervical soft tissues, with fever and pain. (3) Temporary vagus paralysis (in one instance it may have been a laryngeal nerve paralysis). (4) Diffuse punctate cutaneous hemorrhages over ipsilateral face, neck, conjunctivae and retina (transitory). (5) Radiculitis (transitory), cervical roots, from vertebral artery angiog-

* We had one other case in which a very transitory (few seconds) decerebrate state occurred on retrograde injection of 70 per cent diodrast for visualization of the vertebral-basilar-posterior cerebral arterial system. There were no permanent sequellae.

raphy. (6) Both prolonged irritation and paralysis of the cervical sympathetics from extracarotid extravasations of diodrast have been encountered.

Other clinical complications reported in the literature have included thrombosis of the longitudinal sinus and connecting veins;[2] thrombosis of the carotid artery (common and/or internal[8]); severe irritation of the soft tissues of the neck from contrast media injected into them;[1] painful cervical radiculitis; hoarseness due to partial paralysis of the vocal cords (recurrent laryngeal nerve injury and/or injury to the vagus nerve); cervical hematoma with laryngeal stridor (necessitating tracheotomy); and transitory spinal cord symptoms—Brown-Séquard syndrome;[39] urticarial reactions; diffuse punctate hemorrhages in the skin of the face.[41] Löhr[23–25] observed postoperative swelling in the neck with subsequent "Schluck" (aspiration) pneumonia. Dunsmore *et al.*[7] reported a fatal case from hemorrhage into the neck.

DISCUSSION

Most of the above intra- and extracranial complications encountered by us have been reported by others, Moniz[29–31] being one of the first to describe them, and recently Dunsmore *et al.*[7] reviewed a few of these complications. Moniz was all too aware of many of these complications, having encountered them in his search for a suitable contrast medium. Because of the high mortality (2 to 3 per cent) from the use of 25 per cent sodium iodide originally used by Moniz, he introduced thorium dioxide (thorotrast) which became immediately popular on the Continent. However, complications with thorotrast have been reported by Ekström and Lindgren,[11,12] Northfield and Russell,[32] Tönnis,[40] Bodechtel and Wichmann,[2] Ziffren,[43] and MacMahon *et al.*[28] and others.*[10] The radioactivity of thorotrast has been a potential danger (Reeves and Stuck[35] and others) which has limited its use and led Gross†[17–20] to introduce diodrast in 1939. It was recognized very early (Pool[34] and others) that 70 per cent diodrast solution was dangerous and should never be used. Although complications with the use of 35 per cent diodrast solution in cerebral angiography have been recognized by most who have performed many of these tests, there have been only a few reports in the literature emphasizing these untoward reactions. Engeset[14] reported 2 fatalities in a series of 1000 cases and single fatalities were reported by Lysholm (1939),[26,27] Löhr,[24] and Dunsmore, Scoville and Whitcomb[7] (1951). Epileptic fits were noted by Gross[17] (1939), Engeset[14] (1944), Lindgren[21] (1947), Wickbom[42] (1948), Dunsmore *et al.*[7] (1951) and others. Hemiplegia is the more common complication of cerebral angiography and has been reported by Chusid, Robinson and Margules-Lavergne,[6] Dunsmore

* Riechert[36,37] has claimed that many of these reported complications with thorotrast were due to an error in its manufacture and that after this was corrected no complications occurred. It would seem doubtful that this would explain all of the complications. Moniz reported a mortality of 1.3 per cent in 445 patients angiographed with thorotrast (Engeset[14]).

† According to Engeset,[14] perabrodil (identical to diodrast) was used by Torkildsen upon the suggestion of Dale at the University Clinic of Oslo in 1938.

et al.,[7] Olsson[33] and others.[14,42] Other complications have been noted by Suga *et al.*,[39] Dyke,[8] Broman and Olsson,[3,4] Löhr[23–25] and others.[22,33] Of more importance, it would seem, would be to review the causes of these untoward manifestations.

ETIOLOGIC FACTORS

Complications of cerebral angiography are undoubtedly due to several factors, one or more of which may operate in any one untoward incident. These might advantageously be considered separately, such as (1) mechanical and hydrodynamic factors; (2) reflex vasospasm; (3) direct chemical vasospasm; (4) disturbances in blood-brain barrier; (5) introduction of air (embolism) and of (6) blood clot embolism (when the latter form in the needle); (7) sensitivity to the drug; (8) severe dilution of the carotid blood with saline.

(1) The *mechanical factors* may be considered as of etiologic significance in the open method, where the carotid artery is manipulated, lifted up and/or pulled. Some of this force may be transmitted directly to the intracranial vessels; this might cause a movement and rupture of an aneurysm. On the other hand, these same factors (manipulation) may cause *reflex vasoconstriction*, such as also occurs with the introduction of a needle into the carotid (particularly if the internal carotid is pierced or manipulated). We have seen what we have interpreted as very severe vasospasm from manipulation of the vessel and consequent contralateral hemiplegia and unconsciousness. This has been relieved successfully with further procainization of the carotid artery sheath and the carotid sinus and nerve and with the use of vasodilators such as histamine. Recently Roseman[38] has shown electroencephalographic changes following needling of the carotid artery without injection of diodrast. The changes were not unlike those seen in the same patient following the injection of diodrast.

Another *mechanical* or *hydrodynamic* factor is the sudden increased intra-arterial pressure coincident with the injection of 10 to 20 cc. of contrast medium which might cause the rupture of an aneurysm. It is problematic in certain instances whether it is this primary increased intracarotid pressure (if such actually occurs) or the irritation of the contrast medium (diodrast) that causes the convulsion and in turn effects an increased intravascular pressure and rupture of the aneurysm. In any event, death may ensue from this, as was seen in our Case 4, and as reported by Falconer[15] (1951).

Cerebral embolisms—(5) air embolism and (6) blood clot embolism—might properly be considered here as mechanical factors. In at least one of our angiograms we have detected what we believe are bubbles of air in intracranial vessels (basilar artery). This introduction of air is an easy technical error and its avoidance requires close observation of the needle, syringe and connecting tubing when the latter is used. It is our experience that even very small amounts of air may prove troublesome, first in blocking a vessel (resulting in poor or no visualization of the vessel) and second in the production of neurologic signs. Löhr[23–25] suggested that the last 1 or 2 cc. of dye be left

in the syringe, thus avoiding the introduction of any bubbles that might remain in the syringe. He also called attention to the very real danger of coagulation of blood in the needle with embolism as a result. This may be avoided with the repeated or continuous irrigation of the needle with normal saline solution. We have avoided the use of a connecting tube and have used a two-way valve connector (attached to the needle) using the cut-off side when changing syringes, connecting the syringe directly to the valve. More recently we have employed a "multiple valve" and kept the needle open with a continous flow of normal saline.

Christophe[5] has called attention to the work of Hugues and Roskam on the role of emboli arising from the site of needle puncture in the arterial wall in any artery. Their cinematographic study of minor lesions in the mesenteric artery of rabbits disclosed the subsequent formation of minute thrombi which were "carried away five or six times in succession by the circulatory stream before a distinct small thrombus finally begins to adhere." Christophe pointed out that "every intracarotid puncture carries some risk, however great the skill," . . . of cerebral embolism. He suggests that here is the origin of delayed (a few hours) neurologic symptoms following cerebral angiography and that Hugues and Roskam's work may be proof *di visu* that the emboli mechanism is predominantly the important cause of complications in arteriography.

Löhr[23–25] has also called attention to the mechanical effect of periarterial and intramural injection of the dye. Both may cause compression of the lumen to the point of its closure. We have seen one such complication occurring in the "open technique" where the needle was forced into the opposite (posterior) wall of the common carotid while dye was being injected. These angiograms failed to visualize any dye in the carotid or cerebral vessels but dye could be seen in the neck and obviously in the wall of the common carotid artery. No serious aftereffects appeared aside from a very painful neck. The area was procainized and 2 per cent "intracaine" in oil was left about the involved vessel area.

(2) *Vasospasm.* Chemical irritation of the carotid sinus with consequent spasm of the ipsilateral cerebral vessels has received considerable attention from almost every investigator in this field. We have been of the opinion that it is certainly a potent factor and blocking of the cervical sympathetic nerves (stellate ganglion and carotid nerve) with procaine is a valuable aid in avoiding or treating the vasospasm thus incurred. A Horner's syndrome has occurred on several occasions in our series and has been reported by others (Engeset[14]).

Ward and co-workers[16] have shown evidence of various intracranial effects of diodrast by simultaneous observation of the cortical vessels, the measurement of the cerebrospinal fluid pressure and the recording of the brain waves (electroencephalogram). The first effect was that of blanching of the cortex (vasospasm) with associated drop in cerebrospinal fluid pressure of a few seconds' duration. This was followed by a slower rise in cerebrospinal

fluid pressure (lasting a few minutes) and a coincident blushing (vasodilatation) of the cortex. They noted that a seizure pattern in the electroencephalogram was produced in the majority of instances immediately upon injection of the diodrast. In all cases with focal epileptogenic lesions of the cortex gross and startling activation of the epileptogenic focus was produced. These changes lasted for several hours. However, stellate ganglion procainization before injection of diodrast prevented vasospasm but did not alter the subsequent electroencephalographic changes. It was of no little interest that solutions of diodrast warmed to body temperature produced less vasoconstriction.

(3) *Direct stimulation (irritation) of the cerebral vessels* by the contrast medium is believed by many (Moniz, Engeset and others) to be of greatest importance in the appearance of untoward neurologic signs in cerebral angiography. It would seem to us that this does occur and its effect on the cerebral vessels may be prolonged. In one instance in our series in which the ipsilateral carotid sinus and nerve, superior sympathetic and stellate ganglia were blocked with 1 per cent procaine before proceeding with the injection of the dye, there was radiographic evidence of cerebral vasospasm with immediate onset of contralateral neurologic symptoms (hemiparesis). These symptoms tended to disappear immediately with intravenous histamine therapy and in a few hours had vanished. We have used tetraethylammonium chloride (200 to 400 mg.) intravenously and intramuscularly with some success in similar cases but have not found it to be as efficacious as when it was used with intravenous histamine or the latter was used alone. Uihlein[41] has used papaverine hydrochloride, gr. $\frac{1}{4}$, injected into the carotid artery immediately before injecting diodrast and has shown improved arteriolar and capillary filling. We have had limited experience with papaverine and have been favorably impressed with its value except for two instances when it was followed by a precipitous drop in blood pressure and temporary respiratory cessation. All of these untoward signs disappeared in 5 to 10 minutes and we were able to proceed with angiography.

We have already mentioned the work of Ward,[16] confirmed by Roseman,[38] in the matter of vasospasm. Since stellate ganglion procainization prevented the initial vasospasm, this may cast some doubt on the idea of vasospasm from irritation of the cerebral vessels. We are still of the opinion that this may occur in view of clinical observations noted above, namely, evidence of transitory hemiparesis, immediate, in spite of stellate ganglion block and with subsequent use of intravenous histamine with recovery.

(4) *Disturbances in the blood-brain barrier* caused by contrast media (perabrodil, diodrast, sodium iodide) was suggested by Olsson[33] as a cause for neurologic signs and symptoms following cerebral angiography with perabrodil (diodrast). If this occurs, then the symptoms may be consequent to the deleterious effect of the dye on cerebral tissues and to the consequent cerebral edema. This may explain what happened to the patient in our Case 1, who had respiratory failure in less than 2 hours after cerebral angiog-

raphy with diodrast and died on the following day.* That much of the untoward effect is exerted through the breakdown of the blood-brain barrier is now apparent and may be a more appreciable factor than the vasospasm it produces as suggested and experimentally shown by Olsson.† [3,4,33] We must confess that a critical survey of our cases discloses this to be true. In most of our cases with complications coming on after 30 minutes, we can be sure that the use of too great a concentration and/or a total amount of diodrast has broken down the blood-brain barrier. This in turn has produced a severe edema of brain tissue with consequent cellular changes resulting, in several instances, in death of the patient. There no longer can be any excuse for the use of 70 per cent diodrast or for using more than 30 or 40 cc. of the 35 per cent solution of diodrast. We report these cases of complications with some temerity, but at the same time we feel they do substantiate in a clinical way the work of Broman, Olsson and others.

(5) and (6) *Embolisms*, air and blood clot, discussed above as mechanical factors, should be emphasized as ever-present dangers.

(7) *Sensitivity to the drug* does exist and should be tested for in all cases by either the eye or the intravenous tests, or both. In spite of this precaution urticarial reactions have occurred (Sugar *et al.*[39]). Uihlein[41] has called attention to a peculiar punctate hemorrhagic reaction in the face which occurred in three of his patients. We have had two such experiences. These facial skin reactions‡ lasted in one instance a week and in another about 3 days and disappeared without further complication.

(8) *Blood dilution*. This means of producing complications in carotid angiography possibly may be brought about by rapid successive washings through the needle with relatively large amounts of saline with consequent dilution of the blood and transitory cerebral ischemia. We hesitate to mention this since it seems a most improbable cause of cerebral ischemia. However, in one patient it was immediately following repeated 20 cc. saline irrigations through the needle that a transient hemiparesis developed. It is possible that the hemiparesis may have been caused by other factors unknown to us.

Other complications of cerebral angiography have been recorded by various investigators. Sugar and co-workers, in doing percutaneous vertebral (artery) angiography, reported (1) "extravasations of blood and contrast medium which were quite painful and disconcerting"; (2) "brachial plexus root neuralgias due to improper needling in the region of the transverse processes of the cervical vertebra"; (3) "entering of the spinal canal (subarachnoid space) which could be serious if an injection of the dye had occurred": (4) "a transitory Brown-Séquard syndrome" in one patient, the

* Furthermore, it is now the consensus that 70 per cent diodrast solution is entirely too irritating ever to be used in cerebral angiography and we certainly condemn its use.

† Severe cerebral edema and death may also occur after the use of diodrast in the presence of internal carotid and middle cerebral arterial thrombosis, as was seen in Cases 2 and 3.

‡ Similar punctate lesions were present in the conjunctiva, sclera and retina.

mechanism of which seemed obscure but might have been on a reflex vasomotor basis. Engeset called attention to a Horner's syndrome following a percutaneous carotid puncture. We have seen this with the "percutaneous" and "open" methods of carotid puncture and in direct vertebral arterial puncture and in the retrograde carotid method (Moniz, Elvidge[13] and Ecker* [9]) of filling the right vertebral artery. In two instances in which the right carotid was injected retrogradely (and compressed on the cerebral side while the brachial artery was occluded with an inflated blood-pressure cuff) the patients exhibited a sudden cerebellar fit and were unconscious for some 20 to 30 seconds. Excellent radiographic visualization of the vertebral, basilar and posterior cerebral was obtained and the patients recovered completely within 3 minutes. In spite of the probable dilution by the blood of the 70 per cent diodrast, using this method (Elvidge and Ecker's) it became apparent that there, too, we must use only the less irritating 35 per cent diodrast solution. With it we have had no more such alarming experiences.

Lindgren[22] reported two serious complications from percutaneous angiography of the vertebral artery. In one instance the patient became blind for 3 days which was followed by "optic aphasia" for 7 days. Complete recovery ensued. Another patient was dazed and disoriented for 24 hours, followed by recovery. Apparently there were no definite localizing neurologic signs in this case.

INDICATIONS FOR USE OF THOROTRAST IN CEREBRAL ANGIOGRAPHY

We do not care to enter into a discussion of the delayed complications when a radioactive medium, such as thorotrast, is employed in cerebral angiography. These have been well-covered by Stuck and Reeves and others. Nevertheless, we have used thorotrast many times without mishap (except in Case 14) and believe it has certain advantages over the acutely irritating contrast media, such as diodrast. However, we concur with those who would reserve the use of thorotrast for the arteriosclerotic and/or the aged patient. In fact, we would use thorotrast in preference to diodrast whenever there is evidence of any type of degenerative or inflammatory vascular disease. We would urge against the use of diodrast in such instances.

However, immediate complications may occur even with thorotrast. Ekström and Lindgren[11,12] claimed that thorotrast can cause thrombosis and embolism around brain tumors and sometimes in regions quite distant from them. Bodechtel and Wichmann[2] reported thrombosis of the longitudinal sinus following thorotrast angiography resulting in death. The cause of the thrombosis in this case is not clear to us and seems problematic. We have reported the precipitation of transitory hemiparesis and mental confusion in one patient following angiography with thorotrast (Case 14).

Löhr[23–25] emphasized that postoperative swelling in the throat either

* This is a modification of Moniz' original technique in which he punctured the right subclavian artery (open technique) and occluded the vessel distally, thus visualizing the vertebral artery. However Moniz did observe dye in the vertebral artery when the carotid artery was injected.

from the open method or from extravasated thorotrast or other contrast media may cause difficulty in swallowing and result in pneumonia in the aged or debilitated patient. We have seen one instance when heparinization 24 hours after thorotrast carotid angiography caused a hemorrhage into the neck, necessitating tracheotomy.*

THERAPY OF UNTOWARD EFFECTS OF CEREBRAL ANGIOGRAPHY

We have already indicated many of the aids we have used to prevent the occurrence of complications in cerebral angiography and some of the means of treating these complications. In most of the cases we have used repeated stellate and superior cervical sympathetic ganglion blocks with 1 per cent procaine. More recently we have used procaine blocks of the cervical sympathetics before doing angiography and have reduced our incidence of complications. Poppen has ingeniously introduced a small-calibre polythylene tube into the region of the carotid sinus and superior cervical sympathetic ganglion for continuous procainization. We have used this method but the unrestrained patient has on two occasions pulled out the tubing. Continuous intravenous histamine therapy with repeated lumbar punctures has seemed to be of value in several cases. Tetraethylammonium chloride given every few hours, intravenously or intramuscularly, has been of questionable value and the same can be said for "Priscoline" given orally. Transfusions of serum albumin, concentrated plasma and whole blood are used for their osmotic effect to overcome cerebral edema in those patients with prolonged neurologic symptoms. These "osmotic agents" probably aid in improving cellular oxygenation by removal of intercellular fluid. Oxygen by nasal cannula or catheter also seems to be of some value and should be used in all serious complications to aid cellular metabolism. We would not hesitate to do tracheotomy† in the unconscious patient to improve pulmonary ventilation and oxygenation of the bood.

We wish to emphasize that in all patients with vascular degenerative or inflammatory lesions, regardless of the age of the patient, diodrast is contraindicated as a contrast medium for cerebral angiography; until a better medium is found, we would prefer to use thorotrast. Large quantities (over 40 cc.) of diodrast are contraindicated in all cases, for Olsson and others have

* This patient had had an "open method" carotid angiography for a very large aneurysm of the intracranial portion of the internal carotid artery. An attempt had been made to partially occlude (tantalum clip) the internal carotid artery in the neck. After 40 minutes she became hemiplegic and aphasic. The clip on the carotid was immediately removed and she improved. On the following day the hemiplegia became more severe and heparinization was started hoping to prevent further thrombosis in the aneurysm or the carotid. Severe deep cervical diffuse hemorrhage ensued causing respiratory embarrassment. Tracheotomy, transfusion of whole blood, and discontinuance of the heparin were effective.

† Tracheotomy has proven its value beyond a doubt in the unconscious patient with head injury or brain tumor, giving a ready means for aspiration of mucus from the tracheobronchial tree. One of us (KHA) began to use tracheotomy for the unconscious patient in a case of serious head injury in 1944 when it became apparent that not a few unconscious patients were dying from lack of pulmonary ventilation with its consequent cerebral anoxia and increased cerebral edema. We have now utilized it in over 100 patients. Such complications have been avoided since the institution of tracheotomy *in all unconscious patients* when respiratory secretions appear to be blocking, to any degree, the tracheobronchial tree.

shown that large quantities and/or heavy concentrations of diodrast may break down the blood-brain barrier with damage to brain tissue. We cannot emphasize enough the importance of these facts and warn against the promiscuous use of such large amounts of diodrast as were used in some of our cases in which complications developed. The use of mechanical plate changers, such as the "Wampus" of Chamberlain, the Sanchez-Perez machine, or Camp's "rapid hand changing" casette, have greatly reduced the need for larger quantities than 7 to 10 cc. of contrast medium per injection. The newer model of the Fairchild camera (roll film) has further reduced the need for these larger quantities of dye and greatly improved the results obtained.

In the "open technique" of cerebral angiography we would again emphasize the danger of excessive manipulation of the carotid nerve and sympathetic ganglia. The stellate ganglion, superior cervical sympathetic ganglion, carotid sinus and nerve should be infiltrated with 1 per cent procaine before any manipulation is performed. We have greatly reduced complications since doing this.

SUMMARY

The clinical complications of cerebral angiography have been reviewed and the several mechanisms in their production have been discussed. The means of avoiding complications in cerebral angiography are summarized as well as treatment of the complications of cerebral angiography. It is suggested that:

1) Percutaneous angiography is the method of choice and probably is followed by fewer complications.

2) Up to this time thorotrast is the medium of choice in those patients in whom degenerative or inflammatory cerebrovascular disease is suspected.

3) Diodrast, though irritating to the vascular endothelium, is comparatively harmless in low concentrations and small quantities. When diodrast is used, it is of utmost importance to use only the 35 per cent solutions in quantities of not more than 40 cc. (probably less). With the newer mechanical methods of obtaining multiple films and even simultaneously recording views in two planes or more there can be no need for large quantities of these contrast media.

4) The immediate recognition and treatment of the complications are imperative and many times will prove successful.

It has been shown that cerebral angiography is not as yet an altogether innocuous procedure, but it is an important advance and addition to our diagnostic methods in intracranial diseases when it is used with certain precautions and technical skill.

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Addendum

Since this was submitted for publication we have noted three more papers on complications of cerebral angiography:

JONES, R. K. Tumor in the neck produced by thorotrast spilled into the tissues during an arteriography. *J. Neuropath. clin. Neurol.*, 1951, *1:* 313–315.
KRÜCKE, W. Histopathologische Befunde an den Körperorganen nach Arteriographie des Gehirns mit Thorotrast. *Zbl. Neurochir.*, 1950, *10:* 189–199.
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WATER EXCHANGE OF CENTRAL NERVOUS SYSTEM AND CEREBROSPINAL FLUID

EDGAR A. BERING, JR., M.D.*

Neurosurgical Service of The Children's Medical Center and the Peter Bent Brigham Hospital, and the Harvard Medical School, Boston, Massachusetts

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A COMPLETE study of each component of cerebrospinal fluid is necessary before its dynamic physiology can be accurately described. This paper presents a study of its largest component, water. Using deuterium oxide (D_2O, heavy water) as a tracer, a general description has been obtained of the water exchange mechanism between blood, brain, spinal cord and cerebrospinal fluid.

The clinical facts of hydrocephalus prove beyond question the necessity of an intact pathway for the passage of cerebrospinal fluid from the cerebral ventricles to the subarachnoid space over the cerebral hemispheres. However, in spite of the apparently conclusive work of Dandy, Weed and others[1,2,4,5,7,15,16] on the formation and absorption of cerebrospinal fluid, these processes are still imperfectly understood. Though most people regard the choroid plexus as the major site of cerebrospinal fluid formation, evidence that indicates this theory needs revision is steadily accumulating. Wallace and Brodie[13,14] have demonstrated that bromide and iodide ions enter the cerebrospinal fluid from the brain substance, and they identify cerebrospinal fluid formation with this process. They stated that cerebrospinal fluid is interstitial fluid from the brain and does not come from the choroid plexuses. Studies with tracer ions have given this idea considerable support. Greenberg *et al.*,[6] using a variety of radioactive ions, showed that the ions appeared at separate rates in cerebrospinal fluid continually draining from a dog's cisterna magna. Such a state is not compatible with production of a completely formed cerebrospinal fluid either by filtration or secretion. This work suggests that each ion is traveling by free diffusion at its own rate. More recent work with heavy water (D_2O) and radiosodium (Sweet *et al.*[12]) has shown a difference in their appearance time in cerebrospinal fluid, which is incompatible with the theory of total formation of cerebrospinal fluid by the choroid plexuses.

MATERIALS AND METHODS

Deuterium oxide (D_2O, heavy water), used as the water tracer, was obtained 99.8 per cent pure from the AEC, prepared as 0.8 per cent NaCl, sterilized and stored in ampules of convenient size. The analysis of experimental samples was done by densimetric[10] or mass spectrographic[11] methods.

* Senior Fellow in Poliomyelitis for the National Research Council under grant from the National Foundation for Infantile Paralysis.

Studies were made on both humans and animals. All patients studied were from the Neurosurgical Service of the Peter Bent Brigham Hospital and The Children's Medical Center. They included individuals in the normal state as well as those affected by a wide variety of pathological conditions. Monkeys and dogs were used in the animal studies.

The general plan of most of the experiments was an intravenous injection of D_2O as 0.8 per cent NaCl followed by appropriate sampling of arterial blood, superior longitudinal sinus blood, cerebral ventricle cerebrospinal fluid, cisterna magna cerebrospinal fluid, spinal subarachnoid space cerebrospinal fluid and central nervous system tissue (cerebrum, cerebellum and spinal cord). Sampling was always done in such a way with sufficiently small quantities as to maintain a normal physiological state. The amount of D_2O given was approximately 1 cc. per kg., which gave an equilibrium concentration of about 0.15 to 0.25 volumes per cent D_2O.

RESULTS

The Normal State. It is difficult to obtain data on problems of this sort in a normal subject. The cerebral ventricles of most animals are too small to allow adequate sampling, and it is uncommon to find normal persons who require ventricular taps. The "normal" subjects of this study were all patients who had had a unilateral subdural hematoma removed 3 to 6 weeks before the studies were made. At the time of investigation they were considered normal, without evidence of impairment of cerebrospinal fluid circulation.

Following an intravenous injection of heavy water into a normal person, D_2O begins to appear in increasing concentration *simultaneously* in the cerebrospinal fluid of the cerebral ventricles, the cisterna magna and the lumbar subarachnoid space. However, the increasing concentration proceeds most rapidly in the cisterna magna, with the ventricular and lumbar spaces following more slowly until equilibrium with plasma is reached. There is considerable variation in the time required to reach equilibrium; the younger and smaller the subject, the more quickly equilibrium is reached. Once equilibrium between blood and cerebrospinal fluid has been established, D_2O disappears from both at the same rate. Fig. 1 shows the extremes of the observed normal D_2O appearance curves. The other normals showed appearance curves of similar configuration lying between these two.

A convenient way to consider these data is by the use of the half time for any compartment to reach blood D_2O concentration. This will be designated as the "half time." While the range of half times is large and the data are insufficient to determine the normal variation, the half times appear to increase with age. The spread of half times observed in each compartment over an age range of 6 months to 87 years is: cerebral ventricles, 2 to 37 minutes; cisterna magna 1.5 to 6 minutes; lumbar subarachnoid space 7 to 38 minutes. These half times are in good agreement with those reported by Sweet *et al.*[1] for 2 adult males with seizures of unknown etiology. Table 1 presents the

half times of the normals studied, along with similar studies reported by others.

The simultaneous appearance of D_2O in all compartments and the fact that the most rapid appearance is in the cisterna magna, make it obvious that this exchange cannot occur from flow of fluid from the cerebral ventricles.

If the choroid plexuses were the only site of entrance of water into the cerebrospinal fluid, D_2O would appear first and most rapidly in the cerebral

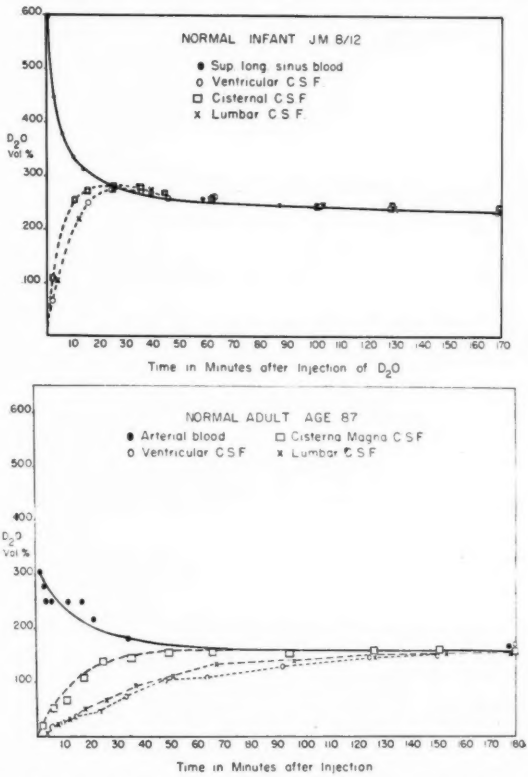

FIG. 1. Extreme range of variation seen in D_2O appearance in cerebrospinal fluid of normal people following intravenous injection of D_2O as 0.8 per cent NaCl.

ventricles. The appearance in the cisterna magna would lag somewhat behind this while the appearance in the lumbar space would be even slower. In such a system the measured rate of cerebrospinal fluid formation of 0.03 to 0.3 cc./min. in an adult[8] would produce a cisternal D_2O appearance half time of over 2 hours as compared to the observed mean of about 3 minutes.

TABLE 1

Normal subjects, intravenous injection of D_2O. Half time for the appearance of D_2O in cerebrospinal fluid of the cerebral ventricles, the cisterna magna, and the lumbar space. Cases from literature are given with those from this study.

Patient	Age (yrs.)	Half Time to Reach Blood Concentration of D_2O			Source
		Cerebral Ventricle	Cisterna Magna	Lumbar Subarachnoid Space	
F. McG.	4/12	7.2 min.	4.3 min.		
E. H.	6/12	6.5 min.	3. min.	18. min.	
J. M.	8/12	2. min.	1.5 min.	7. min.	
W. B.	47		6. min.	38. min.	
M. R.	86	37. min.	5. min.	32. min.	
Adult male		11. min.	1.4 min.	25.5 min.	Sweet *et al.*[12]
Adult male		8.1 min.	1.5 min.	18.6 min.	Sweet *et al.*[12]

Effect of Choroid Plexectomy. The effect of radical bilateral choroid plexectomy has been studied in 2 patients. In spite of radical surgical removal of both ventricular choroid plexuses, no evidence of any alteration in the water exchange could be detected as the pre- and postchoroid plexectomy D_2O appearance curves could almost be superimposed on each other. If the choroid plexus were responsible for a major fraction of the water exchange, the postoperative appearance of D_2O should have been much slower than preoperatively. This is proof positive that the choroid plexuses have at most only a small part in the water exchange of the cerebrospinal fluid of the cerebral venticles. The pre- and postoperative D_2O exchange curves of one of the patients are shown in Fig. 2.

Exchange in the Isolated Spinal Subarachnoid Space. An additional demonstration that the water exchange in the lumbar area is independent of

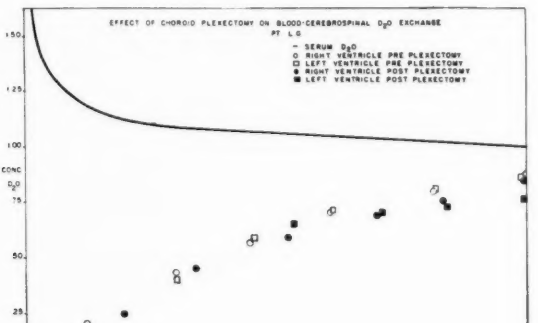
EFFECT OF CHOROID PLEXECTOMY ON BLOOD-CEREBROSPINAL D2O EXCHANGE
PT. L.G.
– SERUM D2O
○ RIGHT VENTRICLE PRE PLEXECTOMY
□ LEFT VENTRICLE PRE PLEXECTOMY
● RIGHT VENTRICLE POST PLEXECTOMY
■ LEFT VENTRICLE POST PLEXECTOMY
150
125
100
CONC D2O %
75
50
25
10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180
TIME IN MINUTES AFTER D2O INJECTION

FIG. 2. The effect of radical choroid plexectomy on the D_2O exchange of the cerebral ventricles.

subarachnoid connections at higher levels was shown by a study of 2 patients with isolated spinal subarachnoid spaces. One had a block of the aqueduct of Sylvius and the other had a block at the level of the foramen magnum (surgically proven). The half times of the lumbar D_2O exchange of these patients were 33 min. and 20 min., which are within the observed normal variation of 7 min. to 38 min. Table 2 and Figure 3 give the half times and appearance curves of these patients as compared to the normals.

TABLE 2

Half time of D_2O appearance in lumbar cerebrospinal fluid following intravenous D_2O into patients with an isolated spinal subarachnoid space

Patient	Age	Diagnosis	Half Time of D_2O Appearance in Lumbar Cerebrospinal Fluid
Infants		Observed normal range	7 –18 min.
Adults		Observed normal range	18.5–38 min.
C. M.	14 yrs.	Block of subarachnoid space at the foramen magnum	33 min.
P. D. B.	14/12 yrs.	Block of aqueduct of Sylvius	20 min.

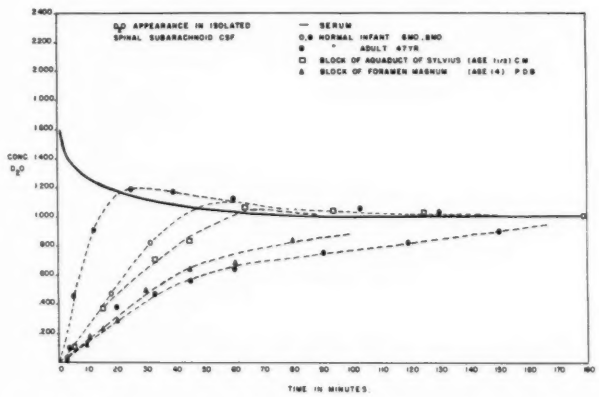

FIG. 3. D_2O appearance in the isolated spinal subarachnoid space following intravenous injection of D_2O.

Comment. The evidence so far presented shows that the choroid plexuses have little to do with the molecular water exchange of the cerebrospinal fluid. It also shows that this exchange takes place more rapidly than can be explained by the flow of cerebrospinal fluid and therefore it is not to be identified entirely with the formation of cerebrospinal fluid. The exchange must take place at the surface of the brain, spinal cord and cerebral ventricles. As any barriers to this exchange must lie in the nervous tissue, it is necessary to investigate the water exchange between blood, brain and spinal cord.

Blood-Brain Water Exchange. The first step in the study of blood-brain water exchange was an examination of simultaneously taken arterial and

superior sagittal sinus blood samples after intravenous injection of D_2O. This was done on 3 monkeys, 8 dogs, and 1 child. No significant arterial-sagittal sinus D_2O difference could be detected. In 1 other monkey an arterial-jugular bulb difference study was done which likewise showed no detectable A-V difference. This result indicated that the transfer of water into the brain was either exceedingly slow or exceedingly rapid as anything between would have shown at some time an arteriovenous difference in D_2O concentration. Fig. 4 shows the arterial and superior longitudinal sinus D_2O concentration curves after intravenous injection of D_2O into a child of 7.

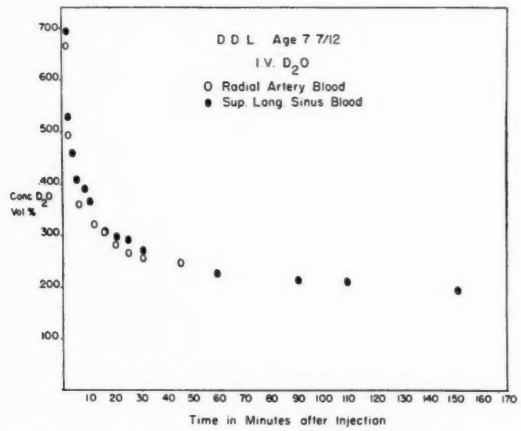

FIG. 4. Blood-brain water exchange. Arterial blood and superior sagittal sinus blood D_2O disappearance curves after intravenous injection of D_2O as 0.8 per cent NaCl into a child of 7.

To clarify the picture, a series of experiments were done to determine the concentration of heavy water in brain and spinal cord tissue following an intravenous injection.

For these experiments dogs were used. Under light nembutal anesthesia, the brain and spinal cord were exposed but the dura was left intact. A rapid intravenous injection (5 to 10 cc.) of D_2O as 0.8 per cent NaCl was given, and after various intervals, from $\frac{1}{2}$ min. to 36 hrs., an arterial blood sample was taken and at the same instant the brain and a section of the spinal cord were removed. The removal was done with a sharp knife cutting through the dura, severing the blood supply and detaching the part as quickly as possible. The time required for this was only a few seconds; about equal to the time required to take the blood sample. If it required more time than the drawing of the blood sample, a second arterial sample was taken. The excess blood was blotted from the tissue, the meninges were stripped off, and the samples were sealed in a dry glass container, quickly frozen and kept in this state until analyzed. In animals where samples were not taken for periods of an hour or more after injection the brain was not exposed until sampling time.

These experiments showed that the D_2O exchange between the blood

brain and spinal cord is free and extraordinarily rapid. The cerebral gray matter and cerebellum were in equilibrium with the blood within a minute after injection of D_2O and the cerebral white matter (corpus callosum) and spinal cord followed a fraction slower, consistent with their differences in blood supply. The amount of blood in nervous tissue is at the most between 5 per cent and 10 per cent by weight; therefore, any increment of D_2O from this source could not have produced this result. It should be noted as a

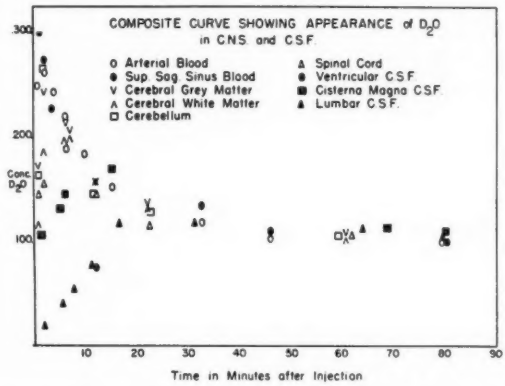

FIG. 5. Composite curve of D_2O appearance in brain, spinal cord and cerebrospinal fluid and of D_2O disappearance from arterial and superior longitudinal sinus blood after intravenous D_2O injection as 0.8 per cent NaCl.

TABLE 3

Time for various portions of central nervous system and cerebrospinal fluid to reach $\frac{1}{2}$ serum concentration of D_2O after intravenous injection of D_2O as 0.8 per cent NaCl. (Dogs)

Tissue	Half Time D_2O Appearance in Dogs
Cerebral gray matter	12 sec.
Cerebral white matter	20 sec.
Cerebellum	12 sec.
Spinal cord	25 sec.
Ventricular cerebrospinal fluid	8 min.
Cisternal cerebrospinal fluid	3 min.
Lumbar cerebrospinal fluid	7 min.

point of great physiological importance that this equilibrium includes all intracellular water as well as extracellular water. The significance of this must await further study, but this exchange is faster than in most other bodily tissues[3].

Fig. 5 shows a composite of the D_2O concentration curves of arterial blood, superior sagittal sinus blood, cerebral gray matter, white matter (corpus callosum), cerebellum, spinal cord (lumbar) and ventricular cisternal and lumbar cerebrospinal fluid after intravenous injection of D_2O. Table 3

records the half times of the D_2O appearance of nervous tissue and cerebrospinal fluid.

Comment. All of the brain water, intracellular and extracellular, is in a free and extraordinarily rapid equilibrium with the water of the blood. The water of the cerebrospinal fluid is continually exchanging at all surfaces of the brain and spinal cord by free diffusion. This exchange is not necessarily to be identified with the formation of cerebrospinal fluid as it involves only one component.

The tracer distribution can be described by a two-compartment model with the blood and brain in one compartment exchanging with cerebrospinal fluid in the other. A mathematical description of the tracer exchange to fit such a model has been developed and will be reported in a separate paper.

DISCUSSION

With the exchange mechanism established, it is well to reconsider the D_2O appearance curves of the cerebrospinal fluid to see why they are to be expected. To help understand them, a general example of changing concentrations will be considered first. In a volume of fluid the rate of increasing concentration of any new substance is a function of the rate of entrance of the substance and the volume under consideration. Any variation of either of these factors, alone or in combination, will change the over-all concentration rate change. For example, 1 gram going into 1 liter in time "t" has an average rate of change of 0.1 per cent/t but if it had gone into only 100 cc., the average rate would be 1 per cent/t. Likewise, if 10 grams had gone into 1 liter, then the rate of increase would be 1 per cent/t; or if the amount is increased to 10 grams and the volume decreased to 100 cc., then the rate is 10 per cent/t.

Returning to the cerebrospinal fluid, if we assume that the water exchange across a given area of nervous tissue is everywhere the same, then the rate of concentration change of D_2O appearing in the cerebrospinal fluid is going to depend upon the ratio of surface area of nervous tissue to volume of cerebrospinal fluid of any compartment considered. Rough approximations can be made of the surface areas presented in the cerebral ventricles, cisterna magna and spinal cord in spite of their irregular shapes.* In an adult the surface area-volume ratio is probably largest in the cisterna magna, less in the lateral ventricles and slightly smaller in the spinal regions. The effect of these differences in surface-volume ratio can be shown by drawing some theoretical appearance curves. This has been done using values of 5, 2 and 1

* The estimations of the surface area-volume ratios were made on the basis of simple geometric equivalents of the lateral ventricles and subarachnoid compartments. The lateral ventricles were assumed to be curved prisms and the spinal region to be concentric oval cylinders. The area presented in the cisterna magna was taken as the surface of the lower medulla plus one-eighth the area of each of two hemispheres. The folia of the cerebellum, which present on the surface as hemicylinders, increase the area by a factor of about 1.5. This correction factor was used in the estimations. These estimations are crude and may not be accurate in magnitude but they provide a suitable working picture of the differences between these regions. The details of these calculations have been omitted for the sake of brevity.

for the surface-volume ratios. These curves correspond qualitatively with the observed curves (Fig. 6).*

More direct confirmatory evidence for the surface-volume effect is obtained from closer examination of the observed data. Any change that occurs in the surface-volume ratio should change the D_2O appearance rate in the compartment considered. If the surface area-volume ratio increases, the half time should decrease and as it gets smaller the half time should increase. In the course of normal growth, the area-volume ratio of all compartments would be expected to decrease.[9] This change should be more in the cerebral ventricles and lumbar region than in the cisterna magna where the large

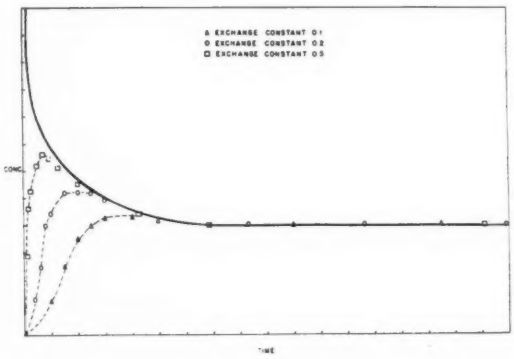

FIG. 6. Theoretical tracer appearance curves drawn with exchange factors in the ratio of 1, 2 and 5. The source curve is equivalent to the D_2O disappearance curve of arterial blood.

area of the exposed cerebellar cortex keeps the area-volume ratio high. This agrees with observed changes in D_2O appearance rates which show increases in the half times with age.

The effects of variation of the surface-volume ratio changes are more clearly seen in the D_2O exchange curves of hydrocephalic patients. A group of 12 infants with various types of hydrocephalus, progressive and arrested, have been studied. All of them showed the expected increase in ventricular D_2O exchange half times as predicted by the decrease of their ventricular surface area-volume ratio which results from the ventricular dilatation. In hydrocephalic children, as in normals, once blood-cerebrospinal fluid D_2O equilibrium has been established, the tracer disappears from both at the same rate. These children are listed in Table 4 with the D_2O exchange half times, diagnosis, state of disease and intracranial pressure. The ventricular cerebrospinal fluid D_2O appearance curves are shown in Fig. 7 along with the slowest observed "normal" ventricular appearance curve.

* Mathematical considerations of these curves will be covered in a subsequent paper describing the mathematics of water tracer distribution in the brain and cerebrospinal fluid.

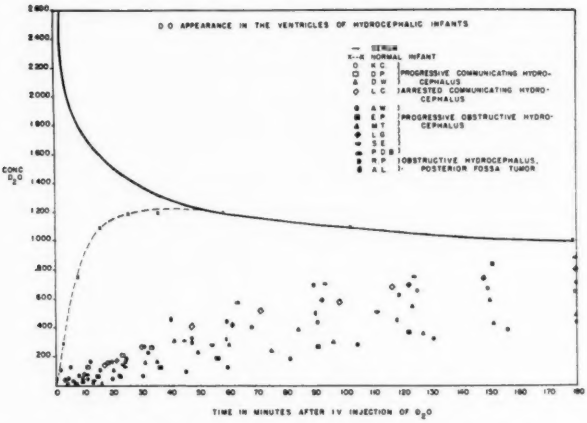

FIG. 7. D_2O appearance curves of the cerebral ventricular cerebrospinal fluid of patients with various types of hydrocephalus, progressive and arrested. D_2O given intravenously.

TABLE 4

D_2O appearance in ventricular and lumbar cerebrospinal fluid following intravenous injection of D_2O into hydrocephalic patients. Appearance is expressed as half time for cerebrospinal fluid concentration to each blood concentration.

Patient	Diagnosis and Clinical State	Age (yrs.)	Sex	Intra-ventricular Pressure mm. H_2O	Half time for Ventricular D_2O Appearance	Half time for Lumbar D_2O Appearance
K.C.	Communicating hydrocephalus, progressive	2/12	F	60	82 min.	
D.P.	Communicating hydrocephalus, progressive	3/12	M	200	Over 245 min.	20 min.
D.W.	Communicating hydrocephalus, progressive	7/12	M	190	89 min.	29 min.
L.C.	Communicating hydrocephalus, arrested	4/12	F	100	73 min.	
A.W.	Obstructive hydrocephalus, progressive	3/12	M	100	Over 180 min.	9 min.
E.P.	Obstructive hydrocephalus, progressive	3/12	M	180	Over 120 min.	
M.T.	Obstructive hydrocephalus, progressive	5/12	M	150	Over 180 min.	
L.G.	Obstructive hydrocephalus, progressive	5/12	F	150	80 min.	
S.E	Obstructive hydrocephalus, progressive	1 3/12	F	60	Over 111 min.	
P.D.B.	Obstructive hydrocephalus, progressive	1 4/12	M	148	60 min.	25 min.
R.P.	4th ventricle tumor with hydrocephalus	10/12	M	120	91 min.	36 min.
A.L.	Posterior fossa cyst with hydrocephalus	1 7/12	M		90 min.	
	Observed normal range				2 to 37 min.	7 to 38 min.

One child (K.C.) with noncommunicating progressive hydrocephalus was observed on constant ventricular drainage to produce about 4 cc. cerebrospinal fluid per hour at a pressure of 128 mm. H_2O. Her ventricles contained between 500–600 cc. cerebrospinal fluid. On the basis of cerebrospinal fluid production, she should have had a D_2O exchange half time of about 3 days. The observed half time was 2 hours, which demonstrates that in the hydrocephalic state total production of cerebrospinal fluid does not account for the D_2O exchange. This clearly demonstrates that water molecules can exchange between the blood, brain and cerebrospinal fluid in spite of an *accumulation* of cerebrospinal fluid. It should be kept in mind that the water

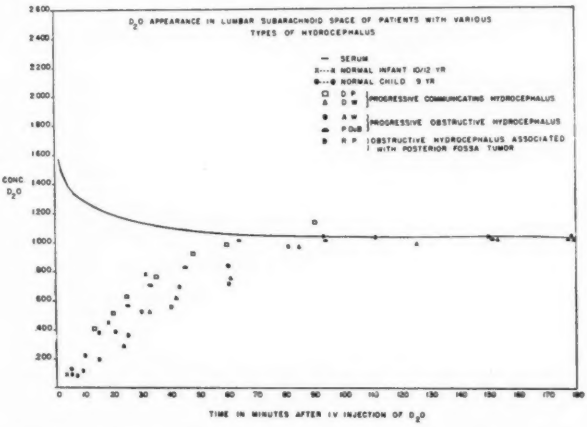
D_2O APPEARANCE IN LUMBAR SUBARACHNOID SPACE OF PATIENTS WITH VARIOUS TYPES OF HYDROCEPHALUS
SERUM
NORMAL INFANT 10/12 YR
NORMAL CHILD 9 YR
D P
D W
PROGRESSIVE COMMUNICATING HYDROCEPHALUS
A W
P D W
PROGRESSIVE OBSTRUCTIVE HYDROCEPHALUS
R P
OBSTRUCTIVE HYDROCEPHALUS ASSOCIATED WITH POSTERIOR FOSSA TUMOR
CONC D_2O
TIME IN MINUTES AFTER I.V. INJECTION OF D_2O

FIG. 8. D_2O appearance in the lumbar subarachnoid space in patients with various types of hydrocephalus The D_2O was given by intravenous injection.

exchange and the accumulation of cerebrospinal fluid are independent phenomena.

The examination of the lumbar D_2O exchange in these patients is of great interest (Table 4 and Fig. 8).

It is not to be expected that the tissue bulk of the spinal regions would change much with hydrocephalus, and as predicted by this, the lumbar exchange half times of the hydrocephalic patients are all very nearly the same and within the observed normal range.

Water exchanges freely and constantly between blood and brain and spinal cord and between the latter and cerebrospinal fluid. Obstructions of the ventricular-subarachnoid pathways have no apparent effect on this exchange except indirectly as the surface area and volume of any compartment are changed. Since water exchange offers no explanation of hydrocephalus or why cerebrospinal fluid must flow, more research is necessary into the ions and large molecules of the cerebrospinal fluid.

SUMMARY

1. The water exchange mechanism between blood, brain and cerebrospinal fluid has been studied in the normal and hydrocephalic brain, using D_2O as a tracer.

2. Water exchange between the blood, brain and cerebrospinal fluid occurs at a molecular level. The accumulation of cerebrospinal fluid is an independent phenomenon.

3. Equilibrium is established very rapidly between the brain, spinal cord and blood following intravenous injection of D_2O. The appearance of D_2O in the cerebrospinal fluid occurs simultaneously in the cerebral ventricles, cisterna magna and spinal regions at a rate that is governed by the surface area-volume ratio of any compartment considered.

4. The choroid plexuses are unimportant in the major D_2O exchange of cerebrospinal fluid.

5. Circulation of cerebrospinal fluid through an intact subarachnoid pathway is not necessary for water exchange into and out of the cerebrospinal fluid, brain or spinal cord.

6. A two-compartment model is mentioned for D_2O distribution into the cerebrospinal fluid.

7. Explanations of hydrocephalus and the necessity of cerebrospinal fluid circulation require more research into the other components of cerebrospinal fluid.

I want to thank Dr. Franc D. Ingraham and Dr. Francis D. Moore for their support and advice which they have generously given to me throughout this investigation.

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DECOMPRESSION OF THE TRIGEMINAL ROOT AND THE POSTERIOR PART OF THE GANGLION AS TREATMENT IN TRIGEMINAL NEURALGIA

PRELIMINARY COMMUNICATION

PALLE TAARNHØJ, M.D.

*Department of Neurosurgery, The University Hospital (Rigshospitalet), Copenhagen, Denmark**

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It is a known phenomenon, described by several authors (Dandy,[1] Mahoney,[3] and Findeisen and Tönnis[2]), that tumours in the cerebellopontine angle may give rise to typical trigeminal neuralgia. In 1949 Olivecrona[4] described a syndrome in which young people with trigeminal neuralgia, affecting or at least beginning in the 3rd branch, had epidermoids in the cerebellopontine angle.

In April 1951, a 31-year-old man with typical trigeminal neuralgia, beginning 3 years previously in the 3rd right branch, was admitted to this department. Because of the patient's age, it was thought that the pain could be due to an epidermoid in the right cerebellopontine angle. This diagnosis was verified by craniotomy, and an epidermoid the size of a hazel nut was found. This caused moderate compression of the trigeminal root. The epidermoid was entirely removed, so that the trigeminal root was completely free. In contrast to previous authors (Dandy,[1] Olivecrona[4]), the temptation to perform simultaneous trigeminotomy was resisted, and the root was left intact.

When the patient woke from anaesthesia he was free from pain and 9 days later he was discharged from the department. At the last follow-up, Nov. 19, 1951, he was still completely symptom-free and had normal sensation in the face.

During the operation and follow-up of this patient, who, with moderate compression of the trigeminal root by the epidermoid, had clinically quite typical trigeminal neuralgia, the idea arose that the cause of the genuine trigeminal neuralgia could perhaps also be sought in a compression of the trigeminal root.

Considering the anatomy of the rather short trigeminal root, it is quite clear that in "normal" anatomical conditions there are few possibilities for compression of the root. However, there is one site where it is possible to imagine that quite small changes in the tissues could give rise to a compression: that part of the root running from the ganglion posteriorly, through the narrow channel formed by the dura, to the upper sharp margin of the petrous bone. Small changes, either in the dura or adjacent tissues, perhaps of vascular origin, could be assumed to narrow the channel so much that a con-

* Chief: E. Busch, M.D.

pression takes place. An increased vulnerability of the root, with increasing age, also seems possible.

If the considerations given above hold good, it should be possible to treat patients with trigeminal neuralgia by dividing the dura over the root without trigeminotomy.

THE MATERIAL

Up to the present a total of 10 patients have been operated on in this way, the first on May 9, 1951 and the last on Nov. 10, 1951. Two of the patients were operated on by B. Broager and the remaining 8 were operated on by the author.

The decompression operation has usually not been performed on any patient who had not had the typical attack of trigeminal neuralgia during the stay in this department. One patient, however, had no pain during the period of observation and was discharged without operation. Fear of future attacks and psychotic depression with suicidal tendencies led to readmission, and a decompression operation (B. Broager) was performed. She had previously had a quite typical trigeminal neuralgia.

Three men and 7 women were operated on. Their ages were 66, 63, 54, 57, 70, 57, 60, 60, 71, and 61 years. The duration of the trigeminal neuralgia was 4, 2, 10, 8, 1½, 7, 17, 11, 5, and 3 years.

Most of the patients had previously, one or more times, been treated with alcohol injections peripherally in the branches of the nerve. The result of this treatment was that 5 of the patients, before operation, had slight changes in sensation and 3 had hypaesthesia with constant burning pain in addition to their typical attacks. Two of the patients were not quite typical, having had pre-operative hypaesthesia in the 1st and 3rd branch, respectively, without alcohol injections. This can perhaps be taken as an indication that the trigeminal root had been subjected to pressure.

TECHNIQUE

The operation is performed through a vertical incision in the temporal region and a small craniectomy. The ganglion is approached intradurally below the temporal lobe. During some of the first operations a small amount of blood seeped from the dura during the opening of the cavum Meckelii, making observation difficult. The technique consequently was modified by plugging the foramen spinosum, extradurally, before the dura was opened. Using this procedure, bleeding has been insignificant.

The cavum can be localized by following the course of the middle meningeal artery, but as a rule it is easier to localize it as the most lateral part of the middle fossa, where the dura is not tightly bound to the base of the skull and feels soft and yielding. The dura over the most posterior part of the ganglion is opened widely, and the trigeminal root is followed posteriorly by dividing the dura above it, until the superior margin of the petrous bone has been reached, and the superior petrosal sinus has been divided between clips. In most cases, the dural incision was continued posteriorly through the edge of the tentorium, so that it was possible to explore the cerebellopontine angle for possible tumours. Care has been taken not to use diathermy in the middle fossa, in order to avoid affecting the ganglion or root, and also

not to cause paresis of the 3rd, 4th, 6th and 7th cranial nerves. In one case only the bleeding made it necessary to use diathermy and this patient had paresis of the facial and abducens nerves. Another patient got a very slight paresis of the trochlear nerve. In a third case the frontal branch of the facial nerve was cut by the skin incision.

RESULTS

Except in the cases just mentioned no complications have been encountered.

On recovery from anaesthesia 3 patients for 1, 2 and 8 days had pain similar to the pre-operative pain. In these 3 patients the operation had been difficult because of disturbing bleeding; they were operated on before the modified technique was developed. The remainder of the patients were free from pain on recovery from anaesthesia. At follow-up, 8, 6, $5\frac{1}{2}$, 5, 3, 3, $3\frac{1}{2}$, $2\frac{1}{2}$, 1 and 2 months after operation all patients were free from their pre-operative pain, both the typical trigeminal neuralgia and the constant burning pain, where the latter had been present. Five of the patients had occasionally insignificant, pricking paraesthesia in some part of the face, usually not with the same localization as the pre-operative pain.

It is still too early to judge the final results; partly because the material is small, and especially because the observation time is too short for a variable disease such as trigeminal neuralgia.

However, I think it justifiable to communicate these observations, since, if the operation proves satisfactory after further examination and in other hands, it should have certain advantages over methods previously used. The main advantage is the absence of anaesthesia with the consequences this may have. At the same time the method appears to have theoretical interest as furnishing some evidence as to the etiology of genuine trigeminal neuralgia.

The disadvantages of the technique described are mainly that the operation presumably means a greater potential risk than the usual temporal trigeminotomy. However, our oldest patient was 71 years of age and stood the operation well. A possibility of secondary scar formation with renewed symptoms should also be mentioned.

SUMMARY

Ten patients with trigeminal neuralgia were treated by decompression of the ganglion and root, without trigeminotomy. The middle fossa was exposed intradurally through a small temporal craniectomy, and the dura was divided widely over the posterior part of the ganglion and root. At follow-up (very short), all patients were free from pain.

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EXTRADURAL CEREBELLAR HEMATOMA

REPORT OF THREE CASES WITH REVIEW OF THE LITERATURE

A. J. BELLER, M.D., AND E. PEYSER, M.D.

Neurosurgical Department, Rothschild Hadassah University Hospital, Jerusalem, Israel

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SEVERAL reports of successful operations in cases of traumatic extradural hematoma in the posterior fossa of the skull have recently been published in the literature. Yet this condition is generally thought to be rare and its symptomatology is as yet ill defined. It is either not mentioned at all or only very briefly in well known textbooks on head injuries.[3,9,19] Since the attention of clinicians has been drawn to this kind of injury by various authors the number of cases observed has increased and the chances of the patient for survival and recovery have improved.

During the last year and a half 2 such cases were seen in our department and another was observed in the Surgical Department of the Rothschild Hospital in Haifa, to which we owe the details. The fact that 3 cases were seen in a relatively short period of time in this country makes us feel that extradural cerebellar hemorrhage must occur more frequently than would appear from the number of published cases. On the basis of our own experience and relevant communications in the literature we wish to outline the symptoms and signs of this disease.

CASE REPORTS

Case 1. A. C., a male aged 18 years, was admitted to another hospital because of brain concussion after he had been kicked by a horse behind the left ear. He had been unconscious for a short time and was still drowsy on admission to that hospital. There was a lacerated wound, 6 cm. long, in the left temporo-occipital region. The underlying bone was slightly depressed. Neurological examination was apparently negative. B.P. was 120 mm. of mercury systolic and 60 mm. diastolic; pulse rate was 72. The wound was excised and sutured and the patient was well the day afterwards. Two days after the injury he again became drowsy and more and more restless. His pulse rate came down to 54 per min. On the third day rigidity of the neck and a positive Kernig sign were noted. The patient vomited twice and his pulse rate fell to 50. Temperature was normal. He became stuporous, and as intracranial hemorrhage was suspected he was transferred to our department.

Examination. The patient was very drowsy; he hardly responded to orders. He had marked rigidity of the neck, increased tonus of the extremities on the left with hyperactive reflexes on the same side, horizontal nystagmus on looking to the left and slight ataxia of the right arm. Roentgenograms of the skull revealed a stellate fracture of the left occipital bone (Fig. 1).

On account of the trauma, the cerebral state of the patient, bradycardia, meningeal and cerebellar signs, a preoperative diagnosis of extradural hematoma in the posterior fossa was made.

Operation. The scalp wound was enlarged posteriorly and a 4×4 cm. depressed fracture of the left occipital bone was exposed. A burr hole was made in the depressed bone, under which old black blood clots were encountered. The whole depressed bone fragment was then removed and about 60 cc. of clotted blood were evacuated. The hematoma was localized in the left posterior fossa mostly beneath and partly above the transverse sinus. After all the clotted blood had been washed out two sources of bleeding were found, one from a small tear in the transverse sinus and the other from the sigmoid sinus. The bleeding was stopped by electrocoagulation and application of gelfoam soaked with thrombin. A small Penrose drain was left in the epidural space for 48 hours and the wound was closed.

FIG. 1. *Case 1.* Stellate fracture of left occipital bone (arrow).

Course. The patient made an uneventful recovery and left the hospital 11 days after operation with no abnormal neurological signs whatsoever. He was seen 5 weeks later entirely healthy and back at his work.

Case 2. S. M., a 27-year-old male, was admitted to another hospital 3 hours after the car in which he was riding had struck a mine. He was found to be very drowsy. His pulse rate was 80 per min.; B.P. was 115 mm. of mercury systolic and 70 mm. diastolic; respiration was normal. There were several lacerations of the scalp, especially in the left occipital region. In addition the patient had closed fractures of the ulna, tibia and 5th metacarpal bone and an open fracture of the 3rd metatarsal bone, all on the left side. No neurological abnormalities could be elicited. X-ray of the skull revealed a starlike fracture of the left occipital bone. The skin lacerations were debrided and sutured and the broken bones were reduced and fixed in plaster of Paris.

The following day the patient grew restless, but no abnormal neurological signs could be detected for the next 6 days, although he never fully recovered consciousness. On the 7th day after the injury his somnolence increased and his temperature rose to 38.5°C. Anisocoria was then noticed and the extremities on the right side were found to be spastic. Since intracranial complication was suspected the patient was transferred to our department.

Examination. He was deeply comatose and responded to very painful stimulation only. The left pupil was larger than the right; both reacted promptly to light. There was no papilledema. He had slight rigidity of the neck, a right spastic hemiparesis and a positive Babinski sign on the right side. Temperature was 39.2°C. and B.P. had risen to 130/70 mm. of mercury.

Operation. Subacute subdural hemorrhage was suspected and burr holes were made in both temporal regions and the left parieto-occipital area. No bleeding was found in either the epidural or subdural space. Although the possibility of a posterior fossa hematoma was considered, no infratentorial exploration was carried out, since anisocoria seemed to rule out a cerebellar lesion.

Course. There was a transitory improvement in the patient's condition the day after the operation, but he again grew worse and died on the 4th postoperative day with signs of medullary decompensation.

Necropsy. There was a large extradural hematoma in the left posterior fossa (Fig. 2) due to a torn transverse sinus (Fig. 3). In addition a small contrecoup laceration of the right frontal pole of the brain was detected, together with a small amount of subdural bleeding in that region.

FIGS. 2 and 3. *Case 2.* (*Left*) Extradural clot found at necropsy over the left cerebellar hemisphere. (*Right*) Tear in left transverse sinus (probe). (Courtesy of the Department of Pathologic Anatomy, Hebrew University-Hadassah Medical School.)

Case 3. F. M. F., an 18-year-old male, was admitted to the Surgical Department of the Rothschild Hospital in Haifa, 24 hours after a big stone had hit his face in a quarry where he had been working. He had immediately lost consciousness.

Examination. The patient was deeply comatose but restless. He did not respond to painful stimuli. There were multiple skin abrasions on his face, and blood came out from his nose, mouth and right ear. There was a large hematoma over the glabella and around the left eye. Pulse rate was 50 per min., B.P. was 140/75 mm. of mercury. Both pupils were round and equal, and promptly reacted to light. There was no rigidity of the neck. No reflexes could be elicited from the lower extremities. Those of the upper extremities were normal. There were no pyramidal tract signs and no lateralizing signs. X-ray films were negative.

Course. During the following night the patient became more restless. His pulse rate went up to 90. His B.P. remained unchanged. The next morning a diagnostic lumbar puncture was performed, which revealed bloody CSF. The patient died immediately after the puncture with signs of respiratory arrest.

Necropsy. There was a fracture at the base of the skull on the left side, extending from the frontal to the occipital bone. There was a large epidural hematoma of about 60 cc. in the left half of the posterior fossa over the left cerebellar hemisphere. The origin of the hemorrhage was a small tear in the external wall of the left transverse

sinus. Both cerebellar tonsils were herniated into the foramen magnum. There were no lacerations in the brain substance.

COMMENT

In a series of 20 cases of extradural hemorrhage McKenzie[15] found 3 cases in which the hematoma extended into the posterior fossa. In one of them it was confined exclusively to that region. LeCount and Apfelbach,[14] in a study on the pathologic anatomy of 504 cases of skull fractures, found 104 extradural hematomas large enough to produce compression. In 8 of them the bleeding had developed in the posterior fossa owing to a tear in the transverse sinus. Fractures of occipital bones, however, were detected in 15 instances. Vance[23] reported necropsy findings in 512 cases of skull fractures. In 61 cases sizable extradural hematomas were found, 4 of them in the posterior fossa.

Thirteen clinical reports of cases in which operation was successfully performed have been presented in the literature.[1,2,4,5,6,8,10,13,20,21,22,24,25] To this series we wish to add our own successful case as the fourteenth.

In Wharton's[25] series of 8 cases of posterior fossa epidural bleeding only 1 patient, with hemorrhage from the torcular, survived. Among the more recent publications Campbell and Cohen's[4] article on epidural hemorrhage in children deserves special notice. Their Case 4 was a newborn boy who had been injured by the application of obstetrical forceps in breech delivery. Neurological signs became manifest 7 days after birth and he was operated upon when he was 2 weeks old. A comminuted depressed fracture of the left occipital bone was debrided and an extradural hematoma, extending from the posterior fossa up over the occipital and parietal lobes on the left, was removed. The patient made an uneventful and complete recovery. In the other cases the bleeding was initiated by a fall on the head or direct injury to the occipital region. The patients were all operated upon within several hours or a few days or weeks after injury. Only Turnbull's[22] patient, representing the chronic form of the disease, underwent surgical intervention 10 months after the initial injury, since a second blow had precipitated neurological abnormalities.

Table 1 summarizes the main clinical features in the cases of extradural cerebellar hematoma in the literature and in our own 3 cases, including those in which the patients did not survive.

External signs of injury in the occipital area were present in all but 4 of the 19 cases summarized in Table 1. This fact has been stressed by Gordy to be helpful in the localization of an extradural clot. There are cases of subcutaneous hematoma with or without skin abrasions, scalp lacerations or even open skull fractures. Immediate loss of consciousness and a free interval, symptoms that are quite characteristic of meningeal artery bleeding, are inconstant in epidural cerebellar hemorrage. About half of the patients were not rendered unconscious by the trauma and one third of them suffered no secondary disturbance of their state of consciousness.

When stiffness of the neck and cerebellar signs are present it is obvious that extradural hemorrhage in the posterior fossa must be considered in the differential diagnosis. However none of them is constant and their absence does not exclude the possibility of such a clot. Indeed they were not found in 9 out of 19 proven cases. Especially cerebellar signs may not be detected if the patient is comatose when seen for the first time or being examined

TABLE 1

Summary of cases of extradural cerebellar hematoma

No.	Author	Year of Publication	Ext. Signs of Injury over Post. Fossa	Immediate Loss of Consciousness	Lucid Interval	Neck Rigidity	Cerebellar Signs	Lateralizing Signs (noncerebellar)	X-ray Findings	Origin of Bleeding	Result
1	Wharton[25]	1901	yes	—	—	—	—	—	—	Torcular	Lived
2	Coleman & Thomson[5]	1941	yes	no	yes	yes	yes	no	yes	Torcular	Lived
3	Gurdjian & Webster[10]	1942	yes	no	yes	yes	no	no	yes	Transv. sin.	Lived
4	Kessel[13]	1942	yes	no	no	—	no	no	yes	—	Lived
5	Turnbull[22]	1944	no	no	yes	yes	yes	no	no	—	Lived
6	Fleminger & Smith[6]	1946	yes	yes	no	no	yes	yes	yes	—	Lived
7	Gordy[7]	1948	yes	yes	yes	no	no	no	yes	Transv. sin.	Died
8	Grant & Austin[8]	1949	yes	no	yes	no	yes	yes	yes	Transv. sin. Torcular	Lived
9	Bacon[2]	1949	yes	yes	yes	yes	yes	yes	no	Dural vessels	Lived
10	Anderson[1]	1949	yes	no	yes	yes	yes	yes	?	—	Lived
11 &	Herren &	1950									
12	Zeller[12]	Case 1	no	no	yes	no	no	yes	yes	Transv. sin.	Died
		Case 2	no	no	yes	no	no	yes	no	Transv. sin.	Died
13	Campbell & Cohen[4]	1951	yes	no	yes	no	no	yes	yes	—	Lived
14	Schneider *et al.*[20]	1951	yes	yes	no	no	yes	yes	no	Transv. sin.	Lived
15 &	Munslow[17]	1951									
16		Case 1	yes	yes	yes	yes	no	yes	no	Transv. sin.	Died
		Case 2	yes	no	yes	no	no	yes	yes	Transv. sin.	Died
17,	Beller & Peyser	1952									
18 &		Case 1	yes	yes	yes	yes	yes	yes	yes	Transv. sin.	Lived
19		Case 2	yes	yes	yes	yes	no	yes	yes	Transv. sin.	Died
		Case 3	no	yes	no	no	no	no	no	Transv. sin.	Died

later on, since their detection depends on the cooperation of the patient. Those are the cases that we wish to point out, since they are easily overlooked.

Occasionally signs are found that seem to indicate a supratentorial lesion. Lateralizing signs like hemiplegia or hemiparesis with unilateral hyperactive reflexes, increased muscle tone or other pyramidal tract signs can be explained by direct pressure on the medulla by the clot or, on the other hand, by the opposite side of the medulla being pressed against the bony ridge of the foramen magnum.

A very important misleading sign is anisocoria, observed in some cases

(Herren and Zeller,[12] Munslow,[17] our Case 2). They show that 3rd cranial nerve involvement may be due not only to herniation of supratentorial structures into the incisura tentorii and pressure on the nerve from above. We have to assume that pressure from below, exerted in the direction of the space above the tentorium, may also encroach upon the nerve.

X-ray findings were positive in about two thirds of the cases (separation of lambda suture, linear fracture of the occipital bone or depressed fracture). They were overlooked in a number of patients who eventually died and on whom necropsy revealed linear fractures of the occipital bone (Bacon,[2] Herren and Zeller's[12] second case, Munslow's[17] first case, our Case 3). There are, however, contrary to the opinion expressed by Munro and Maltby,[16] proven extradural cerebellar hematomas where even at operation no fracture could be detected (Turnbull,[22] Schneider, Kahn and Crosby[20]).

Further information available in suspected cases from a lumbar puncture, e.g. increased cerebrospinal fluid pressure, bloody or xanthochromic fluid, is of no help to the diagnosis. This point has also been raised by Anderson,[1] Coleman and Thomson[5] and by Schneider, Kahn and Crosby.[20] Our Case 3, which ended fatally, shows the danger inherent in lumbar puncture in such cases. It should therefore be discouraged in order to prevent a pressure cone into the foramen magnum, as is the case with other kinds of space-occupying lesion in the posterior fossa.

In spite of the fact that the source of bleeding is usually in the external wall of either the transverse sinus or the torcular Herophili the spreading of the hemorrhage occurs mostly in the direction of the posterior fossa. There are, however, several cases where it was found to extend over the occipital and even the parietal area as well. Guthkelch[11] has recently reported a case in which an extradural clot, originating from a traumatic leakage of the torcular, extended over both occipital lobes, leading to almost total cortical blindness. It did not reach the posterior fossa. The patient completely recovered after evacuation of the hematoma. We do not know why the bleeding spreads in the infratentorial or supratentorial direction or both of them. Possibly gravity (posture of the head) and the degree of adherence of the dura to the bone in different areas play a decisive role. The question of posture has been raised by Coleman and Thomson[5] and by Anderson.[1] They observed that the patient prefers to lie on one side (presumably the side of the lesion). We are, however, unable to confirm this statement.

Papilledema is not found in the acute cases of extradural cerebellar hematoma. It has been observed in the subacute (Bacon:[2] 8 days after injury; Anderson:[1] 12 days) and chronic forms (Turnbull:[22] 9 months) of the disease.

The only chance for cure is offered by surgery. Negative exploratory burr holes in the immediate vicinity of the above-mentioned sinuses in suspected cases do not exclude the presence of a hematoma below the venous sinuses on the same side. We would therefore advocate infratentorial exploration in any case where history and clinical findings arouse suspicion. It is preferable

to perform a number of negative burr hole explorations than to miss a single extradural clot. This rule, which is generally accepted for any suspected bleeding from a middle meningeal artery, applies in the same measure to posterior fossa epidural clots.

CONCLUSION

Epidural bleeding into the posterior fossa of the base of the skull should be suspected in cases of trauma to the back of the head when signs of increased intracranial pressure and abnormal neurological findings, either cerebellar or noncerebellar, appear together after a lucid interval which, however, need not invariably be present. The condition usually develops more slowly than epidural hematomas in the middle fossa since the bleeding is always venous. External signs of injury as well as plain roentgenograms may be helpful in the correct diagnosis and exact localization of the lesion.

Rigidity of the neck and cerebellar signs usually indicate a lesion in the posterior fossa. Pyramidal tract signs, whether homolateral or contralateral, neither exclude nor prove this diagnosis. Occasionally a sign of third nerve involvement (Reid and Cone[18]) occurs and should not lead to the exclusion of an infratentorial lesion. Although no definite explanation of this phenomenon can be given, that of pressure on the nerve from below is most likely.

The only therapeutic measure which may offer success is surgical removal of the clot and sealing off the origin of bleeding.

SUMMARY

Three cases of extradural cerebellar hematoma are presented, one of them successfully operated upon, the other two fatal. The main findings in relevant cases of the literature and our own material are tabulated and clinical features are discussed.

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ANTONY CHIPAULT
1866–1920

D. PETIT-DUTAILLIS
University of Paris, Paris, France

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With the passage of time Antony Chipault, the French pioneer in the field of neurological surgery, appears to us as a strange and sympathetic personality. He was certainly the first surgeon in France who consecrated all his activity on the arduous problems presented in that period by the surgery of neurological affections. Too little known to his compatriots, living and working on the margins of the official medical world, Chipault has left few traces of his personal life. Most of his contemporaries are dead and the rare survivors, whom we have been able to interview, remember him only vaguely. The reason doubtless is that these problems, because of their complexity, interested only himself and left his contemporaries rather indifferent. Most of the information that we have been able to gather concerning him we owe to his wife and adopted son. Thus we know that he was born in Orléans on the 15th of July, 1866. He was of the fourth generation of a line of physicians, and his father, Adolphe Chipault, was surgeon-in-chief to the Hospital of that city.

Having completed his secondary studies at Orléans, he came to Paris as a student of medicine and his surgical vocation was early evident. He was *externe des Hôpitaux* in 1885, *interne* in 1887. He became successively the pupil of Dumontpallier, of Th. Anger, of Trélat, of Saint-Germain, and finally of Professor Duplay, who later attached him to his surgical clinic at *l'Hôtel-Dieu*, in charge of otology and rhinology. During his internship he was *aide d'anatomie* in the medical faculty. He did not follow up, however, these beginnings of his hospital career. Doubtless even then he judged how ungrateful this career was and how little compatible with his interest in investigation. Moreover, his inaugural thesis (one of his best works) on the relationship of the spinous processes to the spinal cord, the spinal roots and the meninges, already clearly showed his orientation towards neurological surgery. And this orientation became ever more accentuated. He began to frequent the neurologic and psychiatric services of the time and entered into relations with renowned neurologists, among them Brissaud, Pierre Marie, Raymond at the *Salpêtrière*, and with psychiatrists, especially Gilles de la Tourette.

One of his contemporaries remembers him as a dry little man, of hardy temperament and imaginative spirit. According to his relatives he was linguistically gifted. He spoke and read easily English, German, Italian, Spanish, Roumanian and even Arabic. He succeeded in translating medical works written in Dutch, Swedish and Russian. In this way he kept himself

abreast of all new developments in various countries concerning his specialty. This explains also how he was able to maintain continuous relations with surgeons all over the world who were interested in neurological surgery, even the most notable of them. He was equally gifted as an artist, as is evident from the numerous illustrations in his writings, which were drawn for the most part by his own hand.

To judge by his writings, the man appears to us a tenacious worker and the type of self-educated and self-made man. His work is scattered through a hundred articles and presentations to the Academy of Medicine, to the Neurological Society, or to different French and foreign Congresses. He assembled each year his personal works and those of his French and foreign colleagues in a volume entitled *Travaux de Neurologie Chirurgicale*, a publication that was a veritable review of the specialty. Besides his contributions to various didactic treatises, he is the author of several books, of which three should be especially noted: *Les Études de Chirurgie Médullaire* (1894), *La Chirurgie Opératoire du Système Nerveux* (1894–95), in two volumes of 700 pages with more than 1,000 figures, and finally, *L'état Actuel de la Chirurgie Nerveuse* in three volumes, the result of a vast international inquiry on the progress accomplished in his specialty and comprising a series of summaries written by the most qualified surgeons in each country. This last work, which must have been very useful at the time, will always be of real interest for the history of our specialty.

The domain of neurological surgery, such as it appeared to Chipault, was very wide, surpassing even the field of neurological affections that might have a surgical indication. He lived in a period when otolaryngology did not exist as a specialty. So we see him passing easily from the surgical treatment of perforating plantar ulcers or peripheral wounds, even Basedow's disease or Pott's disease, to the treatment of sinusitis, of complications of suppurative otitis, or to that of tumors of the spinal cord and brain. In his technical books he did not content himself with giving a description of the different procedures described by the authors. He criticized them acutely on the basis of his own personal experience or precise anatomical researches. So his articles on the surgery of the branches of the trigeminal nerve or of the gasserian ganglion are models of their type. From the point of view that interests us here we may note, among his works, those that treat of surgical affections of the brain and the cord, and also surgery of pain.

Affections of the spine and the cord first retained his attention. Traumatic lesions of the spine first led him to make his exact anatomical researches, an important contribution to the topographic diagnosis of radiculomedullary lesions. This work on the relations of the spinous processes with the spinal cord and the spinal roots has justly remained a classic. He was among the first to establish the operative indications in cases of incomplete paraplegia, of purely radicular symptomatology or of traumatism to the spine. He first imagined, and realized with success, a ligature of the spinal laminae for the maintenance of reduction in certain complicated luxations

ANTONY CHIPAULT

after spinal fractures. He attacked the problem of paraplegia in Pott's disease. At a period when many surgeons advised forcible reduction of the gibbus he deserves credit for protesting vigorously against orthopedic or surgical intervention, showing how rare it was that the mechanism of these symptoms could be reduced to a simple phenomenon of compression and accentuating the importance of vascular phenomena and edema.

Tumors of the spine and spinal cord, aside from metastatic tumors, were rarely diagnosed in his day. At the height of his career he could gather 22 cases of compression of the cord by tumor, of which 15 were malignant tumors of the spine, 5 were extradural and 2 intradural, the histologic nature

of which we do not know. If he obtained in these last cases only one definitive recovery with complete functional return, this fact must be attributed to the late diagnosis and not to the surgeon.

But he was not less interested in surgery of the cranium and brain than he was in that of the spine and the cord. He was interested in cranio-encephalic topography and he has left to us an ingenious proportional procedure destined to give constant results, whatever might be the form of the cranium or the age of the subject. In traumatic lesions his experimental researches with Braquehaye, based on the graphic method, on the mechanism of fractures of the vault and base are well known. He was the first to utilize radiography of the cranium for the location of projectiles. Among the observations reported by him concerning cerebral traumatism, we find some very remarkable for the period and which do honor as much to his clinical intuition as to his surgical audacity. For example, a late case of paraplegia with hematoma between the hemispheres healed by evacuation of the hematoma. Or that other case of epilepsy caused by traumatic porencephaly remaining healed for at least two years following liberation of adhesions and opening of the ventricle.

He declares that he made his first operative attempt for cerebral tumor in 1892 and in 1902 he could assemble a series of 22 operated cases, a notable achievement if one remembers that at the same period W. W. Keen could find only 99 operations by all the surgeons in the United States. If the majority of his interventions were simple decompressive trephinings because of the absence of localizing signs, there were two patients who survived ablation of a hemispheric tumor. The first one, said to have had an angioma of the cortex, was probably, according to the operative description, suffering from a parasagittal meningioma about the size of an orange. The patient was followed for a year after operation. The second observation concerned a patient who had a subcortical glioma and survived operation for three months. "Surgery of tumors of the brain is a sad surgery," Brissaud said at this time concerning a case where the tumor was superficial, well limited, easily enucleable, but not operated upon because of the absence of localizing signs. "The clinic is still sadder," answered Chipault, "which gives only false, vague or too long delayed diagnoses." And he added, "we surgeons are ready from the technical point of view, on the day when the clinicians are able to deliver to us cerebral tumors well localized, not too large or too diffuse. On that day their therapeutic convictions will be established as are ours already. Only surgical intervention can save the patient. It has sometimes done so already and one day will do so much more often." This is the word of a prophet and apostle who retained his faith in the future in spite of the cruel deceptions of the moment.

In the field of the surgery of pain, Chipault reported in his works several radicotomies for pain in the limbs, particularly that accompanying amputation stumps. He studied particularly methods published in his day for the treatment of facial neuralgia. He did not dare to support the resection

of the ganglion of Gasser, which had been proposed by Krause, because of the very high mortality. He remained, for that reason, faithful to peripheral neurotomies, of which he gave a very precise description.

Finally, from a technical point of view, Chipault had imagined various instruments among which were his retractors for laminectomy, his rongeur with flat jaw for the same operation, and his doubly angled chisel for craniotomy. He had understood the utility of wax for hemostasis of bone and used fine sponges for arresting capillary hemorrhage in the brain. He understood the importance of hermetic suture of the dura mater in cases of ablation of cerebral tumor.

When one learns of his scientific production one is astonished at its diversity and extent. He was interested in all the branches of his art. There is nothing that he did not attempt, even treatment of epilepsy by cortical excision. Most surprising is the fact that this production extended over a only short period of eight years, from 1894–1902, for the man was of fragile strength. The immense labor which he accomplished in such a short time seems to have ruined his health. This man who had consecrated his life to neurological surgery (destiny has often such cruel ironies) suffered in 1907, at the age of 41 years, the first signs of a slowly progressive quadriplegia of obscure origin which obliged him to retire from the campaign and to terminate all of his professional activity. Nevertheless, he lived to see the first world war, bitterly regretting that he was unable to devote himself to the wounded. He died at Orchamps, a little village in the Jura, on the 30th of December, 1920, forgotten by his contemporaries. He was, nevertheless, a true precursor of neurological surgery in his country. If he did not find there an audience he had nevertheless the consolation of finding one among his foreign colleagues. He was the only one in his day among his compatriots to believe in the future of cerebral surgery. It is not the least of his merits and is alone sufficient to justify the rehabilitation of his memory.

CASE REPORTS

SCIATICA CAUSED BY TUMORAL CALCINOSIS

A CASE REPORT

PAUL A. RIEMENSCHNEIDER, M.D., AND ARTHUR ECKER, M.D.
State University of New York Medical Center at Syracuse, and The Syracuse Memorial Hospital, Syracuse, New York

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The purpose of this paper is to draw attention to sciatica caused by tumoral calcinosis. It is a rare condition of obscure etiology marked by benign, lobulated, fluctuating, calcified cystic masses in the region of gliding surfaces or bursae. These masses are usually not accompanied by pain, tenderness or limitation of motion. However, in the patient reported the mass of tumoral calcinosis pressed on spinal nerve roots and was the apparent cause of sciatic pain. Removal of the mass was followed by relief of pain.

CASE REPORT

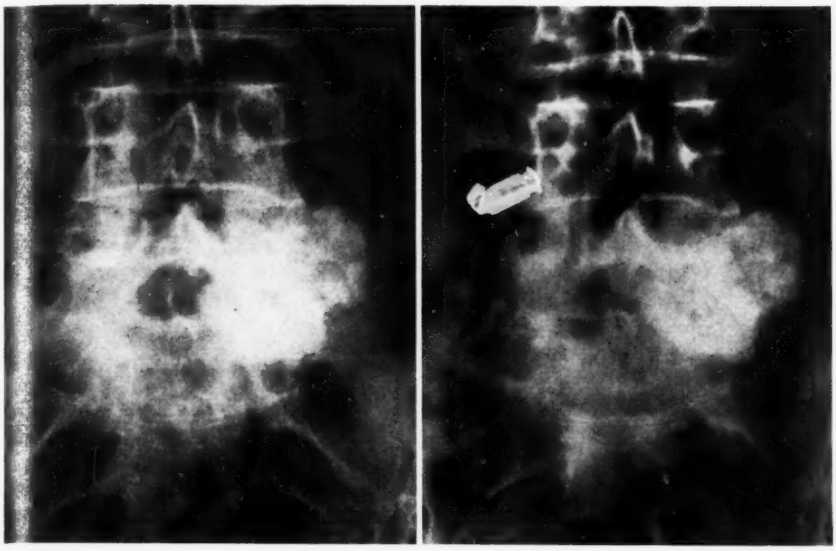
A 59-year-old woman, referred by Dr. Charles Lloyd, complained of pain for 2 years in the left buttock and down the back of the left lower limb to the ankle. One year before we saw her, x-ray studies had revealed a calcified cauliflower-like mass in the left lumbosacral region which measured about 5×3 cm. (Fig. 1). Similar smaller masses were present over the right greater trochanter and in the region of the left subdeltoid bursa. She had never taken vitamin D before these films were made. Subsequently the patient took 2000 units of vitamin D daily for 6 months. The left sciatic pain became progressively more severe several months before admission. It was unaffected by coughing or sneezing. There was neither paresthesia nor difficulty with sphincteric control.

Physical Examination. There was marked impairment of flexion of the lower portion of the lumbar spine with moderate bilateral muscle spasm. The left Achilles reflex was markedly diminished. Straight-leg-raising was permitted to 100° on the right side and to 90° on the left side with pain referred to the left sacroiliac region in each case. There was no weakness of the muscles of the lower limbs and no tenderness along the courses of the sciatic or tibial nerves. Marked impairment of pain sensation was present over the posterior aspect of the left thigh and calf, greater on the lateral than on the medial aspect. This hypoalgesia indicated more involvement in the 1st than in the 2nd sacral dermatome. Vertebral tenderness was sharply localized to the left of the spinous process of the 5th lumbar vertebra. All changes of position were extremely painful. Jugular compression did not increase the pain. Speed of movement of toes was normal. There was no tenderness near the right greater trochanter.

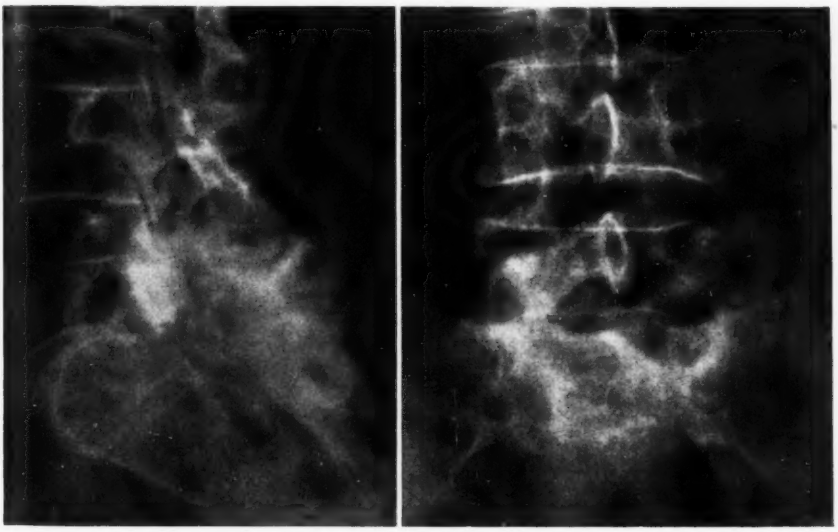
Laboratory Data. Serum calcium was 10.4 mg./100 cc. (normal 9.5–11.0 mg.); total serum phosphorus was 5.3 mg./100 cc. (normal 3–5 mg.); complete blood count was normal; urinalysis was normal except for a trace of albumin.

Roentgenographic Examination (Figs. 2 and 3). Films showed that the cystic calcification was larger than at the original examination. Both anteroposterior and lateral films suggested that the progressive calcification was within the spinal canal, with some calcareous material lying among the nerve roots.

Operation, August 7, 1951. Exploration of the lumbosacral region on the left side revealed a multiloculated mass, lying posterior to and attached to the hemilamina and left transverse process of the 5th lumbar vertebra. There were dense adhesions to the overlying erector spinae muscles. The cysts contained dry, whitish, cheesy material measuring, in all, 6×4×3 cm. The posterior surface of the left side of the sacrum, near the midline, was partially hollowed



FIGS. 1 and 2. (*Left*) A-P view of lumbosacral spine showing irregularly calcified mass overlying the body of the 5th lumbar vertebra. (*Right*) A-P view taken 1 year later, showing progression of lesion particularly towards and across the mid-line.



FIGS. 3 and 4. (*Left*) Lateral view of lumbosacral spine showing calcification both anterior and posterior to the subarachnoid space. (*Right*) Postoperative A-P view showing hemilaminectomy and removal of the bulk of the mass with, however, some scattered portions remaining behind

by the mass. The left hemilamina of the 5th lumbar vertebra and some adjacent bone were removed. Some of the contents of the cysts, apparently spontaneously extruded, lay anterior to the left 1st and 2nd sacral nerves, surrounding them near their posterior ganglia and exerting pressure against them. This calcareous material was easily spooned away. There resulted thorough decompression of both nerve roots. The lumbosacral disk, which was bulging somewhat laterally, was not disturbed.

Microscopic Examination. The material removed was composed of necrotic fibrous tissue and muscle with areas of calcification in the soft tissue.

Course. Convalescence was uneventful and the wound healed primarily, except for an intermittent brown, serous discharge from a pin-point opening in the wound for 2 months. Postoperative roentgenograms (Fig. 4) showed absence of the main bulk of the calcareous material with some remnants left behind. Immediately after operation, the severe low-back and left sciatic pain disappeared. Now, 5 months after operation, the patient is still free from pain.

DISCUSSION

There have been very few reports on tumoral calcinosis.[2,3,4] According to Thomson and Tanner, "Tumoral calcinosis occurs in young individuals of both sexes. There is probably a familial tendency. The tumors are large, rapidly growing to a definite self-limited size; they usually occur in or near bursal sites, near large joints, and in connective tissue, immediately overlying bone and muscle attachments. The tumors are hard and lobulated, have fairly well-defined limitations in contour, are attached firmly to underlying deep structures and may show some infiltration into the muscles. There is usually no pain, tenderness, or limitation of joint motion. There is a definite multilocular cystic arrangement of the tumor, which has thick rubbery walls, showing inflammatory foreign body giant cell reaction. Deep cystic areas are filled with calcareous material and some milky fluid."

Deposits of calcified, fluctuating cystic masses have been ascribed to vitamin D intoxication, especially when associated with an unusually high calcium intake.[1] Such cases associated with excessive vitamin D intake may represent tumoral calcinosis on an exogenous basis while others, including our own, may have an endogenous metabolic defect as their cause. It is conceivable that both types have an endogenous defect but that some patients require, in addition, the action of massive doses of vitamin D as a catalyst before the pathologic calcification can be produced.

By roentgen examination the lesions of tumoral calcinosis are easily visible. They consist of single or multiple cyst-like areas of calcification in the regions of bursae and muscles. Many of the individual lesions cannot be differentiated from calcific bursitis. In aggregate, the lesions radiographically and pathologically are probably in all respects similar to those described after massive doses of vitamin D. Occasionally a single lesion may bear a superficial resemblance to an exostosis but adequate examination should demonstrate amorphous calcification rather than the trabecular structure of ossification. There is also a lack of stalk attached to the underlying bone.

It seems probable that vitamin D was unrelated to the pathogenesis of symptoms in this case. It is likely that one or more of the cysts ruptured and that the extruded contents within the spinal canal caused pressure on the 1st and 2nd sacral nerves a few months before the patient was referred to us.

SUMMARY

A case of low-back and left sciatic pain with the clinical syndrome of a protruded intervertebral disk was caused by tumoral calcinosis. The symptoms were apparently

the result of pressure by extruded contents of the cystic mass on the 1st and 2nd sacral nerves within the spinal canal. The symptoms were promptly relieved by operation.

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TORULOSIS OF THE BRAIN

A CASE REPORT

Frank Padberg, M.D., and John Martin, M.D.

Department of Surgery, Northwestern University Medical School, Chicago, Illinois

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Recent literature has produced numerous reports of patients with torulosis of the central nervous system. Carton and Mount[1] reviewed the literature and recorded 42 patients upon whom neurosurgical procedure had been performed. We have treated 1 patient who had torulosis. The diagnosis was established only after diagnostic trephination. The patient received penicillin and sulfadiazine medications as well as other general supportive measures, but such did not alter his rapidly progressive neurological deterioration which ended in death.

CASE REPORT

Summary. Mr. J. J., a white farmer, 28 years old, came under our observation on Nov. 23, 1946. He had a history of a head injury with slowly progressive neurological signs thereafter. Diagnostic trephination for a subdural hematoma was done, but no such lesion was found. The small scalp incisions both soon became indurated and in a few days broke down and suppurated. Yeast organisms were identified in the discharge from the operative wounds as well as in the spinal fluid. At autopsy he was found to have a generalized torulosis.

History. This patient gave a history of a minor head injury in October 1946 as his only clue to diagnosis on admission to the hospital. He had been in excellent health prior to this accident and was actively engaged in hard labor. The injury was not followed by immediate complaints. Two weeks after the injury he had an attack consisting of a sudden onset of faintness, numbness in the right hand and arm, inability to use the right hand and twitching movements about the face. Following this attack he complained of frontal headache and pain in the cervical spine. He had four or five such attacks, each lasting approximately 30 minutes, and none was associated with unconsciousness. His headaches and neck pain, at first intermittent, became constant and increasingly severe. In the early part of November 1946, he complained of diplopia, dimness of vision, weakness of the right hand and arm, and some difficulty in speech.

The patient had served with the U. S. Army Air Corps for 3 years and had been stationed in Guatemala, France, Italy and Trinidad. His only significant illnesses had been measles and mumps in his childhood and pneumonia several times during his youth.

Examination. B.P. 120/80, temperature 99.6°, respirations 18 per min., and pulse 72 per

min. The patient was quiet and alert. His neck was moderately stiff and painful on passive manipulation. There was a slight right facial weakness and a mild weakness of the extremities on the right. He was right-handed and showed a slight motor aphasia. He had a bilateral papilledema with many fresh and old hemorrhages. The left pupil was dilated and slowed in its reaction to light. The extraocular muscle movements were well performed and there was no nystagmus. The right abdominal reflexes were absent. The right cremasteric reflex was diminished. There were no pathological reflexes.

A spinal puncture was done with the patient in the lateral recumbent position and the spinal subarachnoid pressure was above 600 mm. of water. WBC was 15,200; differential blood smear showed 2 eosinophils, 78 polymorphonuclear cells, and 20 lymphocytes. The CSF

FIG. 1. Coronal section of brain through the occipital lobes. This transects the local softened abscessed areas under each trephine opening. The ventricles appear to be partially collapsed.

was clear, but total protein content was 58.8 mg. per cent, and there were 2 polymorphonuclear cells and 30 lymphocytes per c.mm. Roentgenograms of skull and cervical spine showed no fractures.

Operation. On Nov. 24, 1946, diagnostic trephine openings were made bilaterally. The brain on the left side was purple in color and promptly herniated when the dura mater was opened. The brain felt soft to the cannula and attempts to cannulate the left ventricle were not successful. Ventricular pressure on the right did not appear to be greatly increased.

Course. The patient continued to have severe unremitting headache and he gradually became somnolent. Three days after surgery a 4 cm. fluctuant swelling developed over the left anterior scalp incision. This was aspirated and a small amount of pinkish-yellow, thick, lumpy material was obtained, which, on direct smear, revealed numerous yeast cells. Spinal puncture was repeated, and the xanthochromic fluid yielded yeast cells on direct examination of the sediment. The CSF sugar was reduced to 8 mg. per cent without change in the normal value for chlorides. Yeast cells were cultured from both CSF and the wound exudate, and on examination the organism was identified as Cryptococcus neoformans, or Torula histolytica.

He had several episodes of fever to 103°, associated with signs of increasing intracranial pressure. He continued a progressively downward course. Kernig and Brudzinski signs were markedly positive. Generalized muscular weakness and atrophy developed with paralysis of the right arm and leg initially which was followed by paralysis of the left arm. No pathological reflexes were ever elicited. He became progressively disoriented, blind, unresponsive, then comatose, and he expired on Dec. 30, 1946.

This patient received 20,000 units of penicillin every 3 hours and 1 gm. of sulfadiazine every 4 hours throughout his hospitalization. The remainder of his treatment was symptomatic. Smears and cultures of urine, blood, nasopharynx, and sputum were all negative for Cryptococcus neoformans.

Autopsy. The cerebral cortex was dotted with many 2 mm.-sized pale green translucent

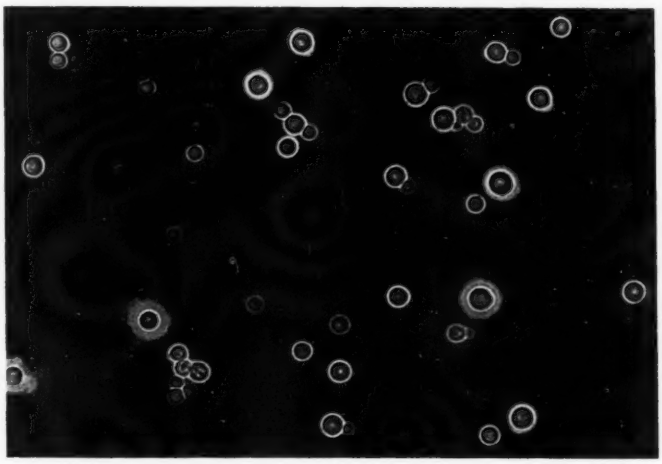

FIG. 2. India ink wet mounts of Cryptococcus neoformans (×700) taken from culture (brain heart infusion agar). Budding is demonstrated.

tubercle-like lesions. In the region of the trephine openings the friable brain had herniated and there were locally shaggy accumulations of exudate and necrotic brain tissue. Sections of the brain through the trephine sites showed areas of softening, greenish-red in color, which extended into the white matter (Fig. 1).

Microscopic Examination. The meninges were infiltrated by round cells, and showed fibrous-tissue hyperplasia in fields where there were many large giant cells surrounded by mononuclear cells, lymphocytes and a few polymorphonuclear leukocytes. Sections of the brain from a softened area in the left occipital lobe demonstrated collections of yeast cells in clumps and chains (Fig. 2). In this area the normal histologic architecture of the brain was lost, but in close proximity to this area the appearance was normal. Surrounding the localized collections of torular organisms, there were a few clumps of lymphocytes and mononuclear cells. There was no evidence of active gliosis in the areas of softening where the torular organisms were seen in the greatest concentration.

Microscopic sections of the kidneys, lungs and spleen had occasional giant cells. Some of the giant cells contained round and oval refractile bodies which were suggestive of yeast cells.

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MULTIPLE SPINAL CORD MENINGIOMAS

ROBERT W. RAND, M.D.

Department of Surgery, Section of Neurosurgery, University Hospital, Ann Arbor, Michigan

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In most large series of neoplasms of the spinal canal, spinal cord and its leptomeninges, the meningioma group comprises approximately 25 per cent. Occasionally a meningioma of the spinal cord is associated with multiple neurofibromas or multiple intramedullary ependymomas. The incidence of multiple meningiomas is small when compared with the frequency of their single occurrence, and in most instances of multiplicity they are intracranial[5,6] or intracranial and spinal.[10] Certainly the examples of multiple meningiomas confined exclusively to the spinal cord are rare,[3] which leads the author to present the following case.

REPORT OF A CASE

Removal of meningiomas from the 6th and 3rd thoracic cord segmental levels respectively. Recovery.

H. D., a 34-year-old white woman, was admitted to the University Hospital on March 12, 1951, because of progressive loss of sensation and of weakness in her lower extremities. A year prior she had noticed "tingling" in her feet which soon progressed to complete and constant "numbness." During June 1950 she became unsteady in walking with occasional episodes of "buckling" of her knees. The weakness in her legs also progressed, being greater on the right. One month before admission her right foot dragged constantly although she could still walk unaided. During January 1951 an "aching pain" developed below the right scapula which was provoked by coughing or lying down; however, this pain did not radiate in a segmental distribution. Coincidentally she noticed the absence of sweating over the lower extremities, and a mild degree of urinary urgency and frequency developed.

Examination. The patient was a well developed, slightly obese female appearing neither acutely nor chronically ill. There was a complete loss of pain and temperature sensation below the 7th thoracic dermatome except for sparing over the sacral segments bilaterally. Deep pain sensation was absent in the legs. Sense of motion and position was normal but that of vibration was diminished below the 8th thoracic segment and was absent at the ankles. Discriminatory touch was impaired below the level of analgesia. Reaction to the Romberg test was positive. Marked weakness of the legs, especially on the right, with associated mild spasticity was noticed, although the patient was still able to walk without help. The deep reflexes of the lower extremities were equally hyperactive with bilaterally unsustained patellar and ankle clonus; abdominal reflexes were absent and Babinski's sign was present bilaterally. Sweating was absent below the 7th thoracic dermatome.

Roentgenograms of the chest and the entire spinal column appeared normal. Following a lumbar puncture, which revealed a complete block to jugular compression, a myelogram was done using 2½ cc. of pantopaque. This demonstrated the block to be at the midportion of the 5th thoracic vertebra with sharp projections of the pantopaque anteriorly and posteriorly in the lateral view (Fig. 1). No CSF was withdrawn at the time of the lumbar puncture for fear of increasing the paresis. Routine studies of blood and urine revealed nothing abnormal.

1st Operation. A laminectomy under intratracheal general anesthesia was performed on March 15, 1951, removing the lamina and spines of the 4th, 5th, and 6th thoracic vertebrae. At the level of the 5th thoracic vertebra the dura was seen to be bulging and the extradural adipose tissue was absent. After opening the dura in the midline, a tumor was evident on the right pushing the spinal cord posteriorly and to the left (Fig. 2). It was attached ventrolaterally by a sessile base to the dura at the level of the 6th thoracic spinal cord segment. The

arachnoid was opened and the well-encapsulated tumor delivered from beneath the spinal cord. Following the removal of this tumor the cord slowly assumed its normal position. When an attempt was made to pass a small, soft rubber catheter cephalad beneath the dura, an obstruction was encountered at the level of the 3rd thoracic lamina. Accordingly the laminectomy was carried upward enough to expose the point of block and upon opening the dura here a second neoplasm was disclosed. It also was attached to the dura by a sessile base but in a dorsolateral position on the left (Fig. 2). The spinal cord at this site, following removal of the

FIG. 1. Lateral view of myelogram showing complete block at site of lower meningioma (5th thoracic vertebra).

FIG. 2. Artist's illustration showing location of the meningiomas at the left 3rd and right 6th thoracic spinal cord segments respectively.

mass with its attached dura, appeared normal with only minimal compression as compared to the spinal cord at the site of the first tumor. The catheter was subsequently passed superiorly into the cervical region and no further obstruction was met. The dura was left open and the wound closed.

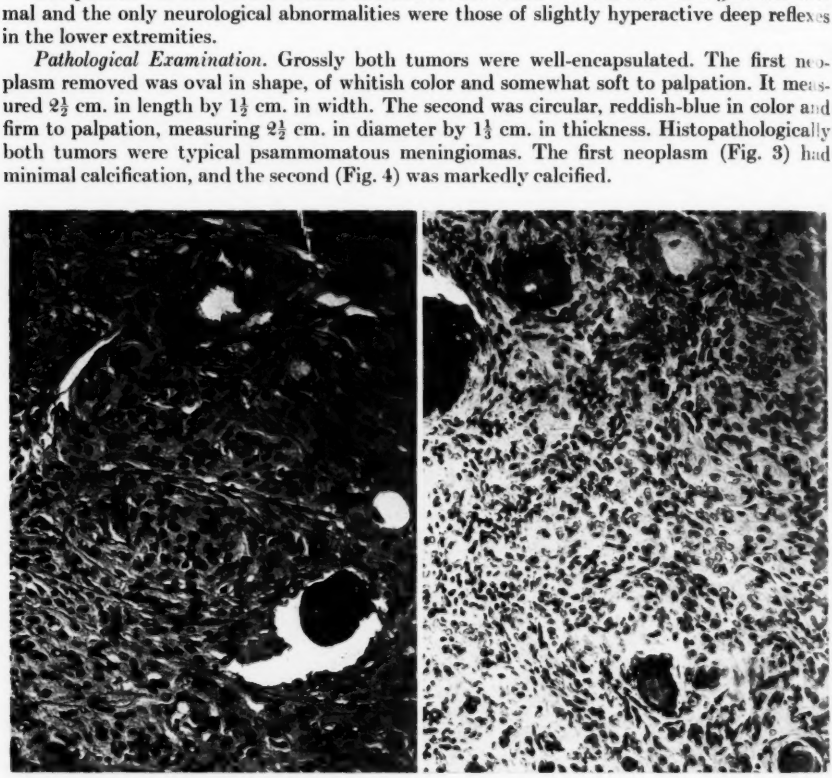
Course. Forty-eight hours after operation the paresis increased and progressed to complete paralysis with loss of all sensory function below the 7th thoracic dermatome.

2nd Operation. Re-exploration of the spinal cord was performed on March 17, 1951 because of the possibility of postoperative hemorrhage. There was no hemorrhage but marked edema of the spinal cord was present at the site of the lower tumor. The subarachnoid space above this was filled with clear spinal fluid.

Course. Two days following this procedure the patient was able to move the toes of her left foot. Function slowly returned and at the time of discharge, April 29, 1951, she was walking with a slightly spastic gait. Bladder function was normal as shown by cystometric studies. Vibration sensation was absent at the ankles; all other sensory functions had completely returned. The reflexes were hyperactive with a sustained ankle clonus on the right. Babinski's sign was not present.

The patient has since led a normal and active life. When last examined her gait was normal and the only neurological abnormalities were those of slightly hyperactive deep reflexes in the lower extremities.

Pathological Examination. Grossly both tumors were well-encapsulated. The first neoplasm removed was oval in shape, of whitish color and somewhat soft to palpation. It measured $2\frac{1}{2}$ cm. in length by $1\frac{1}{2}$ cm. in width. The second was circular, reddish-blue in color and firm to palpation, measuring $2\frac{1}{2}$ cm. in diameter by $1\frac{1}{3}$ cm. in thickness. Histopathologically both tumors were typical psammomatous meningiomas. The first neoplasm (Fig. 3) had minimal calcification, and the second (Fig. 4) was markedly calcified.



FIGS. 3 and 4. Photomicrographs of the psammomatous meningiomas found (*left*) at the right 6th thoracic spinal cord segment, and (*right*) at the left 3rd thoracic spinal cord segment. Hematoxylin-eosin stain, ×16.

COMMENT

The term "multiple meningioma" was coined by Cushing[5] to designate discrete neoplasms of the brain without coalescence. In our patient the spinal cord meningiomas were discrete with normal dura and arachnoid intervening. Multiple intracranial meningiomas are frequently associated with von Recklinghausen's disease. Kernohan[9] has suggested that the histologic appearance of meningiomas in the presence of von Recklinghausen's disease may be atypical and resemble neurofibromas. The tumors in this instance were typical psammomatous meningiomas (Figs. 3 and 4) and the patient presented no stigmata of neurofibromatosis.

It is believed that meningiomas develop from nests of arachnoidal cells scattered throughout the dura and, further, that the syncytial or "meningothelial" type develops from the "cap" cells of the arachnoid, although the fibrous type arises from the fibrous elements of the arachnoidal meshwork.[1,4] The majority of meningiomas

of the spinal cord occur in females, and 70 to 80 per cent[7,11] of all such tumors are located in the thoracic region. The explanation for the predominance of these neoplasms in women and in the thoracic region is obscure.

Since the introduction of myelography, many cases of successful removal of multiple neurofibromas with complete recovery have been reported;[8] however, surgical removal of multiple meningiomas of the spinal cord is rare. The clinical and roentgenological findings in this case clearly indicated a solitary tumor at the 5th thoracic vertebral level. The sensory level was quite definite at the 7th thoracic dermatome with no evidence of disturbance superiorly. The myelographic study would have demonstrated other tumors caudal to that found at the 6th thoracic spinal cord segment, even though the clinical symptoms of a lower lesion might have been obscured. The multiplicity of the lesions was clinically unsuspected in this case—the second meningioma being the silent partner. At times multiple lesions are recognized only when new symptoms develop. One should bear in mind that intraspinal meningiomas may simulate degenerative diseases of the spinal cord.[2] This patient was sent to the University Hospital with the presumptive diagnosis of multiple sclerosis.

The surgical management of multiple meningiomas is not unlike that of solitary tumors. In this instance, because of the severe compression of the spinal cord caused by the first neoplasm lying somewhat anteriorly to the cord, a partial intracapsular excision was performed before any attempt was made to lift the tumor from its bed. The second meningioma was easily removed as it presented dorsally to the spinal cord. In spite of this technique, severe edema of the spinal cord occurred resulting in complete paraplegia 48 hours postoperatively. Although delayed, recovery was complete.

When dealing with spinal cord neoplasms the possibility of concealed, asymptomatic, multiple tumors must be kept in mind and a high index of suspicion maintained. After the removal of a neoplasm, further exploration of the spinal canal should always be made by passage of a catheter. Myelographic studies should be carried out several weeks postoperatively if the results of the operation do not come up to expectation.

SUMMARY

A case is presented of the removal of two separate meningiomas of the spinal cord which were not associated with von Recklinghausen's disease.

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NOTICES

AMERICAN NEUROLOGICAL ASSOCIATION

The 77th annual meeting of the American Neurological Association will be held at the Hotel Claridge, Atlantic City, New Jersey, from May 8 to 10, 1952.

CENTENAIRE DE PIERRE MARIE

The 100th anniversary of the birth of Professor Pierre Marie will be celebrated in Paris on July 9, 1952. A group of his former pupils will describe his principal contributions. The program includes the following: G. Guillain: Sa vie scientifique .... Percival Bailey: L'acromégalie. L. van Bogaert: L'amyotrophie Charcot-Marie. Th. Alajouanine: L'aphasie. I. Bertrand: L'hérédo-ataxie cérébelleuse. J. Thiers: La pathologie cérébelleuse .... J. Lhermitte: L'oeuvre anatomique et anatomopathologique .... Guy Laroche: Le pathologie osseuse .... J.-A. Barré: La spondylose rhizomélique. M. Patrikios: Ses travaux pendant la première guerre mondiale. P. Behague: Pierre Marie intime.

Those who wish to attend the celebration are asked to communicate with M. P. Behague, 4 Avenue Belle-Vue, Le Chesnay, (S.-et-O.).

SCANDINAVIAN NEUROSURGICAL SOCIETY

The 8th meeting of the Scandinavian Neurosurgical Society will take place in Stockholm, Sweden (Serafimerlasarettet and Södersjukhuset), September 19–21, 1952. On September 21 there will be a joint session with the Symposium Neuroradiologicum. Members of American and other European neurosurgical societies are cordially invited to attend. Information is obtainable from the Secretary, Dr. Olof Sjöqvist, Södersjukhuset, Stockholm, Sweden.

THIRD SYMPOSIUM NEURORADIOLOGICUM

The third Symposium Neuroradiologicum will be held in the Riksdagshuset (Houses of Parliament), in Stockholm, September 17–20, 1952. Leading specialists from Britain, Canada, France, Germany, The Netherlands, Italy and Sweden will read about 30 papers concerning the roentgenological diagnosis of lesions of the brain and the spinal cord. Among the subjects to be discussed are: Radiological diagnosis of spinal tumours. Vertebral angiography. Encephalography in tumour cases. Tomography in neuroradiology.

Scientific and technical exhibitions will be arranged. A social programme is planned. Programmes and application forms may be obtained from: Secretary of Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K, Sweden.

THE CEREBELLAR ANGIORETICULOMAS

H. OLIVECRONA, M.D.

Neurosurgical Clinic, Serafimerlasarettet, Stockholm, Sweden

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THE angiomatous tumors occurring in the cerebellum have been variously designated as angioreticulomas and angioblastomas, and are also commonly referred to as Lindau tumors, since Lindau's[5] important contribution in 1926 brought the attention of neurosurgeons to this, in the adult, fairly common type of cerebellar tumor. Since the term angioreticuloma appears to be best adapted to the histological appearance of these tumors, I have in accordance with Bergstrand[1] used this designation.

Although arteriography has brought out a surprising number of arteriovenous aneurysms, it is nevertheless true that angiomatous malformations

TABLE 1

Verified intracranial tumors up to Dec. 31, 1950

Glioma	2,008	47.9%
Meningioma	806	19.2%
Neurinoma	356	8.6%
Adenoma	368	8.7%
Angioma	111	2.6%
Arteriovenous aneurysm	104	2.5%
Aneurysm	77	1.9%
Craniopharyngioma	74	1.9%
Cholesteatoma	31	0.9%
Teratoma, chordoma	10	0.2%
Papilloma	17	0.4%
Granuloma	55	1.3%
Metastatic	147	3.5%
Miscellaneous	24	0.6%
	4,188	

and tumors of the brain are comparatively rare lesions. In the earlier statistics of such as Cushing and Bailey[3] (1928) and Cushing[2] (1932), blood-vessel tumors, in which group are included the true tumors as well as the angiomatous malformations, made up about 2 per cent of the verified brain tumors. In the statistics of this clinic up to Dec. 31, 1934,[1] the corresponding figure was 3.5 per cent, the larger figure in this clinic probably being due to the extensive use of arteriography. In Table 1 are assembled the verified brain tumors observed in this clinic up to Dec. 31, 1950. As may be seen, the angioreticulomas are somewhat less numerous than the arteriovenous aneurysms and make up approximately 2 per cent of our verified tumors. This may seem to be an insignificant number, but when it is recalled that the angioreticulomas occur only in the cerebellum of adults, it becomes

obvious that they form an important group of cerebellar tumors. In Table 2 are assembled the 958 verified posterior fossa tumors observed in this clinic up to Dec. 31, 1950. The angioreticulomas comprise 7.3 per cent of the total number of posterior fossa tumors.

TABLE 2

Age incidence of posterior fossa tumors
1922–Dec. 31, 1950

	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80
Gliomas (408)	175	108	57	34	21	10	3	
Acoustic neurinomas (349)	0	6	52	81	89	89	31	1
Meningiomas (75)	0	2	5	18	26	19	4	1
Angioreticulomas (70)	0	6	13	14	14	20	3	
Tuberculomas (22)	2	6	11	3	0	0	0	
Metastatic (16)	0	1	0	2	7	4	2	
Papillomas, cholesteatomas, chordomas, teratomas (22)	0	2	8	6	4	2	0	

PATHOLOGICAL ANATOMY

From the now classical descriptions of Cushing and Bailey,[3] Lindau[5] and others, the histological appearance of these tumors is well known and need not detain us here. The macroscopical anatomy of these tumors as they appear at the operating table is as a rule sufficiently characteristic to allow a correct diagnosis as soon as the lesion is seen. The tendency to cyst formation, so typical of these tumors, has been emphasized by all. Tumors unaccompanied by cysts are by no means rare and sometimes the cysts are quite small although they are generally of a size many times the solid tumor nodule. Lindau[5] found 2 entirely solid tumors among his 16 cases, and in the material of Cushing and Bailey[3] cyst formation was lacking in no less than 4 out of 11 cases. In our material of 70 cases there were 55 cystic and 15 solid tumors, the solid tumors thus comprising 18.4 per cent of the entire series. If to this group are added the cases in which the cyst was quite small, we find that in between one fourth to one third of the cases, cyst formation was lacking or was so small as to be without significance. It would seem, therefore, that the frequency of cyst formation has been somewhat overemphasized in the earlier literature.

The mural nodule in the cystic tumor may occasionally, as pointed out by Cushing and Bailey,[3] be quite small, so small in fact that it can be detected only by microscopical examination of the cyst wall, but as a rule it is easily recognized and varies in size between that of a pea and a walnut. In one of the rare cases where a true recurrence was thought to have occurred, the originally cystic tumor was later replaced by a large solid mass, occupying the entire cerebellar hemisphere of one side.

Since these tumors in all probability take their origin from a meningo-

cerebral malformation, the mural node in the cystic tumors and the solid tumors are always located close to the surface of the cerebellum or the medulla and it will be found that they are always at some point in direct contact with the pia-arachnoid. They are therefore in most instances easily detected at operation, even when unaccompanied by a cyst. The exceptions are those cases in which no cyst is present and the solid tumor is located far anteriorly, close to the superior surface of the cerebellum, which may not always be accessible to inspection. Even in these cases the vascular pattern seen on the surface of the cerebellum usually gives a clue to the presence

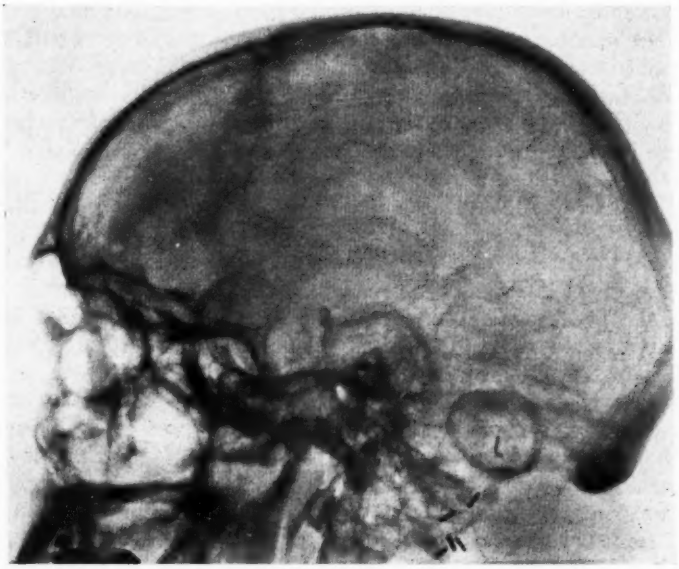

FIG. 1. Vertebral angiogram in a case of right-sided cerebellar angioreticuloma. The tumor was largely solid, although accompanied by a small cyst.

and location of the tumor and it is exceedingly rare that the tumor is not found at operation. The increased vascularity of the cerebellar cortex near the tumor is very characteristic and almost pathognomonic. One or several branches of cortical arteries are greatly enlarged and converge towards the tumor and the draining veins are several times the size of normal cerebellar veins and often contain bright red arterial blood. When the solid tumor is large, the vascular supply may be so abundant that the lesion becomes almost aneurysmatic in appearance. In angiograms of the vertebral artery the vascularity of these tumors can be beautifully demonstrated (Fig. 1).

In our material the tumor was localized to the cerebellar hemispheres in 56 cases, to the vermis in 9 cases and to the region of the fourth ventricle

in 5 cases. In the last-mentioned group the tumor usually arises from the velum medullare posterius, which separates the tumor from the floor of the fourth ventricle. This situation obtained in 1 of our cases reported in our monograph with Bergstrand and Tönnis[1] in 1936. In 2 other cases the tumor had its point of attachment to the medulla in the region of the velum medullare posterius, but the exact relations of the tumor to the velum could not be determined. In 1 case the tumor was located to the uppermost part of the fourth ventricle, growing in a ring-like fashion around the lowest part of the aqueduct, and apparently attached to the floor of the fourth ventricle at its cranial end. In the fifth case there were 2 tumors, one probably arising from the velum medullare posterius but rather firmly attached to the medulla in the region of the calamus scriptorius, and the other attached to the lateral margin of the fourth ventricle, just above the striae acusticae. The opinion generally expressed in the literature that the angioreticulomas located to the region of the fourth ventricle always arise from the velum medullare posterius therefore no longer can be sustained.

HEREDITY—RELATION TO v. HIPPEL'S ANGIOMATOSIS RETINAE—MULTIPLE TUMORS

Familial occurrence of angioreticulomas has been recorded in the literature on several occasions. When associated with angiomatosis retinae, cysts of the pancreas and tumors of the kidney, the condition generally goes under the name of Lindau's disease. Heredity is frequently, though not invariably, observed in this condition.

On the whole, the combination of angiomatosis retinae with a cerebellar angioreticuloma is very rare and the hope once expressed by Cushing and Bailey that this combination might in the future be of considerable diagnostic importance has not been fulfilled. In the present series angiomatosis retinae was observed only once among 70 cases. Perlmutter, Horrax and Poppen[7] recorded the unusually high frequency of 16 per cent of angiomatosis retinae among their 25 cases.

In this clinic 3 families have been observed in which 2 or more members of the family were afflicted with angioreticulomas. Norlén[6] made one of these families the subject of a short report in 1941. The pedigree of this family is reproduced from Norlén's paper.

♀ Died, 44 years old, from brain tumor

No. 1	*No. 2*	*No. 3*
♀, 37 years old. Multiple cerebellar angioreticulomas removed 1937, 1940, 1941.	♂, 25 years old. Died, cerebellar angioreticuloma.	♂, 25 years old. Living, well.

No. 1	*No. 2*	*No. 3*	*No. 4*
♀, 18 years old. Multiple cerebellar angioreticulomas removed 1939, 1942.	♀, Died at birth.	♀, 13 years old. Living, well.	♂, 10 years old. Living, well.

In the second family the patient was a man aged 34 at the time of his first admission. His mother had died at the age of 56 from hypernephroma with multiple metastases to the lungs. She had been suffering for some months from a cerebellar tumor which was thought to be metastatic. At autopsy, however, it was found that the cerebellar tumor was an angioreticuloma situated in the roof of the fourth ventricle. The patient himself had three different angioreticulomas in the cerebellum, two of which were removed at the first operation in 1947 and the third at a second operation 2 years later. Two of the tumors were situated in the fourth ventricle and one in the right hemisphere. His present condition indicates that he may have still another angioma in the cerebellum.

In the third family, the patient was a man aged 46. His mother became blind at the age of 23. One brother died from brain tumor, and another brother was operated on for brain tumor, diagnosis unverified. One sister has blindness in the left eye, caused by angiomatosis retinae. The patient himself has bilateral angiomatosis retinae, which was first diagnosed in 1941 and which led to blindness in both eyes. Signs of intracranial hypertension began late in 1949 and he was operated on in November 1950, when a large cystic angioma was removed from the left cerebellar hemisphere.

It was characteristic in all 3 cases of familial occurrence that multiple tumors were present, although usually only one tumor was manifest at a time and years elapsed before symptoms of intracranial disease again became apparent. Obviously it is well to keep patients with a hereditary tendency under close observation, as new tumors in other parts of the cerebellum are very likely to occur. The last-mentioned case was the only one in the present series in which angiomatosis retinae was found.

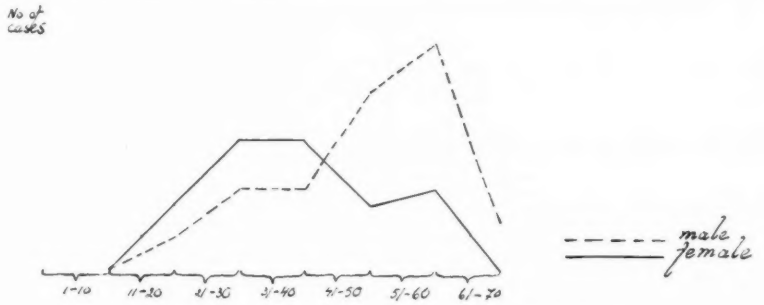

FIG. 2. Age and sex incidence of cerebellar angioreticulomas.

SEX AND AGE INCIDENCE

There were 41 males and 29 females in our material, indicating a slight preponderance for the male sex. The age distribution presented in Fig. 2 suggests that the tumors tend to manifest themselves at an earlier age in the female than in the male sex. In the female, the greatest incidence occurs

in the age group 20–40, while in the male the maximum frequency occurs two decades later. No case occurred before puberty and only 8.7 per cent of the patients were below 20 years of age when the first symptoms were noted. The age distribution is not without diagnostic significance as the vast majority of cerebellar gliomas occur before the age of 20 and most of these before puberty.

SYMPTOMATOLOGY

The first symptom nearly always is headache, which was recorded as the initial symptom in 59 cases or in 84 per cent of the entire material. In 42 cases vertigo appeared almost simultaneously with headache or very shortly afterwards. Vomiting occurred very early in 29 cases.

The headache nearly always is of the type associated with intracranial hypertension but occasionally may occur in a more unusual form as in one of our cases, in which the first symptom was a sharp pain in the occipital region, provoked by stooping or the lifting of heavy burdens. Vertigo may occur in attacks resembling Ménière's disease but is more often described as periodically recurring sensations of giddiness, frequently associated with bouts of increased headache. In some instances, vertigo is so intense that disturbance of gait and station occurs permanently at an early stage or as one of the initial symptoms. Although by no means pathognomonic, the combination of headache, vertigo and vomiting occurring as the earliest symptoms is a fairly reliable indication of a posterior fossa tumor.

In rare cases some unusual symptom may initiate the disease. In one case, failing vision because of angiomatosis retinae was the first symptom and in another case mental symptoms resembling a frontal lobe syndrome were the first symptoms to be observed. The evolution of the disease is quite variable and in our material, the length of history before admission varied between a few weeks up to over 2 years. About two thirds of our patients came under neurosurgical care within a year after the appearance of the first symptoms. The history is apt to be shorter and the appearance of severe symptoms, particularly signs of foraminal herniation, tends to occur earlier in the younger patients, and a protracted course is perhaps more often seen in the elderly patients. There appears to be no connection between type of tumor, whether cystic or solid, or location, and length of history.

The onset is usually gradual but occasionally a very sudden onset of severe symptoms has occurred. In one case, in which the tumor had not been found at the first operation and only a suboccipital decompression had been made, hemorrhage into the tumor precipitated a pressure syndrome of extreme severity. The course before admission to a neurosurgical clinic is apt to fluctuate somewhat, with remissions alternating with periods of more severe symptoms. Occasionally fairly long remissions may occur but in most cases there is a gradual but steady increase in the severity of symptoms.

At the time of admission all patients complained of headache. Vomiting

had occurred in 55 cases or 80 per cent. Choked disc was found in 63 cases; normal eyegrounds were present in only 6 cases. In 1 case, the eyegrounds could not be seen because of secondary changes in the media, following angiomatosis retinae. Four patients were blind at the time of admission, 1 because of angiomatosis retinae, the other 3 because of choked discs with secondary atrophy. Visual acuity was more or less affected in 18 cases. In about one third of the cases, therefore, increased intracranial pressure had existed long enough to affect visual acuity. Evidence of foraminal herniation in the form of cerebellar fits was present in 14 cases and in an additional 8 cases stiffness of the neck was found, although cerebellar fits had not yet occurred. Bulbar symptoms in the form of hoarseness and inability to swallow occurred in 2 cases; both patients died before operation could be performed and these symptoms, as well as other evidence of foraminal herniation, are therefore to be considered as a sign of utmost urgency. Other common symptoms of intracranial tension were double vision, usually temporary, in 17 cases and paralysis of upward conjugate movements of the eyes in 7 cases.

A syndrome of intracranial tension was therefore found in every case and it was well advanced in a large number of cases. Long-standing intracranial hypertension found its roentgenological expression in the form of erosion of the posterior clinoids, increased convolutional markings, etc. in 18 cases. In the early days before the extreme urgency of these cases was recognized, especially when cerebellar fits made their appearance, no less than 5 patients died before operation could be performed and 1, also in the ultimate stage of medullary compression, died in the general surgical clinic after an operation for pleural empyema.

Among the localizing symptoms, disturbances of cerebellar functions are the most frequent and important. Cerebellar disturbance of gait and station was found in 56 cases, asynergia and hypotonia, usually one-sided, in 34 cases, and nystagmus in 29 cases. Unless appearing early before severe intracranial hypertension has set in, disturbance of gait and station is of little localizing value, as any patient who has been severely ill and bedridden for some time is apt to be more or less unable to walk. Among the cerebellar symptoms only nystagmus is of greater localizing value in those cases in which signs of intracranial tension have been present for some time.

Palsies of cranial nerves are not infrequent. Weakness of the facial nerve, usually homolateral, was observed in 15 cases. Homolateral decrease of hearing occurred in 2 cases. More often homolateral tinnitus is observed; this symptom, which is rarely permanent but usually occurs in short periods, was observed in 6 cases. Sensory disturbance in the field of the trigeminal nerve was found in 10 cases: in 2 cases these changes were bilateral; in 8 they were one-sided and located to the side of the lesion. Although double vision occurs frequently, palsies of the 3rd, 4th and 6th nerves are rare; only occasionally has an abducens palsy been observed.

DIAGNOSIS

A cerebellar syndrome with severe pressure symptoms, particularly signs of foraminal herniation, in an adult person having a history of less than a year is quite suggestive of an angioreticuloma. However, many other tumors, especially tumors of the brain stem, pinealomas and sometimes even tumors of the cerebral hemispheres, may give rise to a similar syndrome and it is therefore altogether unsafe to rely upon the neurological findings alone. The presence of angiomatosis retinae would of course clinch the diagnosis but this condition is so rare that it is devoid of practical value for the diagnosis of cerebellar angiomas. Contrast roentgen examination is therefore necessary to substantiate the diagnosis.

Of our patients who underwent surgery, only 3 were operated on without previous air studies of any kind. In 1 of these cases, a cerebellar cyst had been found at operation in another hospital some years earlier; in the other 2 the diagnosis was based upon the neurological findings alone. These were early cases, however, and increasing experience has convinced me that apparently typical neurological syndromes can lead to diagnostic errors which in critical cases are very apt to lead to disasters. Therefore, in every case in which there is the slightest doubt, it is advisable to substantiate the diagnosis by ventriculography.

Lumbar encephalography is definitely contraindicated when a cerebellar angioma is suspected, unless one is prepared to operate immediately. However, since the encephalograms in such cases are very likely to be negative because no air enters the ventricular system, this principle cannot always be followed. Should this be the case it is advisable, if pressure symptoms exist, to follow up the procedure immediately with ventriculography and operation. Otherwise the lumbar puncture might provoke a fatal foraminal herniation.

Suboccipital puncture and air injection was attempted in 9 cases in which a cerebellar angioma was unsuspected. In 2 of these, the needle struck a cyst in one of the herniated tonsils and the diagnosis was established by filling the cyst with air. In 1 case a cyst had been tapped through a suboccipital puncture in another clinic but no air had been injected. In the remaining 6 cases either no fluid was obtained or the injected air did not penetrate into the ventricles. Ventriculography was subsequently performed in these cases and the tumor was verified and removed at operation. Although no harm resulted in any of these cases which were thought suitable for suboccipital air injection because the symptoms of intracranial tension were mild, suboccipital puncture in cases of cerebellar tumors is attended by a definite risk, particularly when the tumors are angiomas, because the needle might easily strike a dilated blood vessel in one of the herniated tonsils.

Air injection after tapping the ventricles is by far the safest and also the most reliable method for establishing the diagnosis of cerebellar angioma. It must be emphasized, however, that ventriculography must be followed

by immediate operation, otherwise the procedure is extremely dangerous. In 2 of our early cases, the importance of immediate operation was not yet appreciated and the patients both died within 24 hours from the increase in pressure following air injection. In another case, in which ventriculography had been performed 24 hours earlier in another hospital, the patient arrived in the neurosurgical clinic in a moribund condition with a temperature of over 40°C. and Cheyne-Stokes respiration. Immediate operation and removal of the tumor failed to save the patient from the effects of this ill-advised ventriculography. In the remaining 59 cases in which operation was subsequently carried out, ventriculography was performed without incident and definitely established the position of the tumor. Sometimes when the tumor is very large no air enters the fourth ventricle and the exact position of the tumor in the posterior fossa may be in doubt. Angiograms of the vertebral artery may then be very useful for completing the diagnosis.

A specific indication for vertebral angiography arises in cases of familial occurrence of angiomas. Experience shows that multiple tumors are frequently present in these cases and angiograms may succeed in disclosing the presence and location of multiple tumors, a fact that ventriculography is quite unlikely to unearth, and which may easily escape attention at operation.

TREATMENT

The operative procedure has not changed much in recent years, but modern methods of anesthesia have contributed materially to the ease and smoothness of its performance. Local anaesthesia has been used in the majority of our cases and this is still the preferable method when the patient is in an advanced stage of intracranial hypertension. If general anaesthesia is used, ether should never be employed because its vasodilative action may increase the volume of the brain so much that, in spite of ventricular puncture, there is insufficient room in the posterior fossa for the manipulations attending removal of the tumor. This is of less importance if there is a large cyst present, but when the tumor is largely or entirely solid and of some considerable size, it is necessary to have all the room one can get, particularly if the tumor is situated in an awkward position high up under the tentorium. Intubation is of course essential in any form of general anaesthesia and the anaesthetic to be used should be nitrous oxide and oxygen combined, when necessary, with pentothal or nembutal. A method that has recently been introduced by Gordh[4] in this clinic is to combine a high spinal anaesthesia with general anaesthesia. The reduction of blood pressure associated with spinal anaesthesia gives more room in the cranial chamber than any other method and also reduces hemorrhage. The blood pressure can be easily controlled by tilting the table in the appropriate angle. This method has not yet been tried in a case of angioma, but has been used to great advantage in operations on acoustic tumors and other tumors in the posterior fossa, and is considered in this clinic as a method of considerable promise.

Although a unilateral exposure might be sufficient in many cases of angioma, a bilateral exposure is always made in this clinic. The reason is that if some complication causing the intracranial pressure to rise occurs during operation, for instance hemorrhage into the tumor or respiratory embarrassment, it may be impossible to enlarge the dural opening with sufficient rapidity to accommodate the swelling cerebellum and great damage may occur before conditions in the operative field are again under control. The arch of the atlas is of course always removed, as a foraminal herniation is almost invariably present. If a cyst is present, this is opened widely and it is then usually easy to remove the mural node. The solid tumors present a much more difficult technical problem. They are usually large and vascular and when situated in an awkward place, they may be difficult to remove. It is seldom of use to try to remove the contents of a solid tumor with the electric loop; it is always much too vascular for this procedure. It bleeds very easily at the slightest touch and before beginning to mobilize the tumor, it is well to expose it as fully as possible by removing the adjacent cerebellar tissue by suction. If it is in a reasonably accessible position, it can then gradually be mobilized and the entering blood vessels clipped as more and more of the tumor is brought into view. When situated on the superior surface of the cerebellum it may be impossible to see and clip the entering blood vessels and this difficult situation is best handled by rapidly enucleating the tumor with brain spatulas and then clipping the blood vessels afterwards when the tumor no longer obstructs the view. After careful hemostasis the dura is closed by interrupted stitches, no attempt being made to make the closure water-tight.

In cases where the tumor is situated high up under the tentorium, an approach from above might be preferable to the usual cerebellar exposure. This was done in one of our cases, where the tumor was located to the superior part of the vermis, extending upwards to the quadrigeminal plate. A large occipitoparietal flap was made, the tentorium was split and the tumor, which was entirely solid, was removed without much difficulty.

RESULTS

In 6 cases, the patients died before operation could be performed. Two of them, both early cases in the series, had been subjected to ventriculography and died within 24 hours from increased intracranial pressure. In the remaining 4 cases, death occurred suddenly shortly after admission. These patients were all admitted in a late stage of intracranial hypertension; they all had typical cerebellar fits. Under present-day conditions they could probably have been saved by immediate ventriculography and operation, or by ventricular drainage during the days preceding operation.

In 2 cases suboccipital decompression was performed. In one of these, a very large, entirely solid and very vascular tumor was found high up in the vermis. The tumor was thought to be inoperable, and after biopsy the operation was terminated as a decompression. He died the same day,

probably from loss of blood and the effects of intracranial tension. Autopsy showed a large midline tumor, extending to the quadrigeminal plate in the cranial direction (Fig. 3). This tumor could probably have been removed from the transtentorial approach. In the other case, no tumor was found at operation. Angiography some days later showed the angioma to be located high up under the tentorium in the right hemisphere (Fig. 1). The patient refused a second operation and did very well for more than a year, when he had a sudden hemorrhage into the tumor and was brought to

FIG. 3. Autopsy specimen of large mid-line angioreticuloma.

the clinic in a comatose condition. At the second operation a large solid tumor, accompanied by a small cyst, filled with recent clot, was removed from the superior surface of the right cerebellar hemisphere. The patient made an uneventful recovery but is still, almost a year after the second operation, unable to work because of cerebellar disturbance of gait.

In the remaining 62 cases the tumor was completely removed. There were 10 fatalities in this group, giving a mortality of 16.1 per cent. Altogether therefore, 64 patients were operated on with 11 fatalities, giving a mortality of 17.2 per cent. As might be expected, the tumors located to the floor of the fourth ventricle carry a very high mortality, the operation having terminated fatally in 2 out of 5 cases.

Five patients came to operation in a comatose condition and died within a day or two because of the combined effects of long-standing intracranial

tension, operative shock and loss of blood. Two patients died of meningitis after particularly long and difficult operations. Two died from the effects of a postoperative clot and 2 from pulmonary complications, pneumonia in one case and pulmonary embolism in the other. These results are not very brilliant, considering the fact that the cerebellar angiomas are benign tumors, on the whole favourable for surgical removal. Unfortunately many of these patients arrive in a neurosurgical clinic in a desperate condition, due to the severity of intracranial tension. It should also be noted that this report covers the experience of the author, such as it was, and that of several of his younger co-workers, during a period of almost 30 years. With earlier diagnosis and modern methods of diagnosis and treatment much better results may be expected in the future.

SECONDARY OPERATIONS

In the 3 cases in which familial occurrence of angioreticulomas was observed, new tumors appeared some years after the first tumor had been removed. In one of these, three tumors in different parts of the cerebellum were successfully removed, the first operation having been performed in 1937 and the last in 1949, and in her daughter a second angioma in the other cerebellar hemisphere was removed 3 years after the first operation. In the third case, two angiomas in different locations had been removed at the first operation and 2 years later still another tumor was removed, also in a different part of the cerebellum. As already mentioned, his present condition indicates that he may have still another angioma somewhere in the cerebellum.

In 2 other cases additional tumors occurred, but since they were localized to the same cerebellar hemisphere, it is impossible to say whether they were true recurrences or new tumors. In the first of these, a cyst-forming angioma was removed from the left cerebellar hemisphere in 1934; the removal was thought to be radical. In the beginning of 1938 another angioma in the same hemisphere was removed, but this obviously recurred very rapidly because at the third operation 10 months later a very large tumor, also in the left hemisphere and almost filling the entire posterior fossa, was removed, this time with an early fatality. At autopsy in this case multiple angioreticulomas in the kidneys were found, indicating a tendency to phakomatosis. In the second case, a cyst-forming angioma was removed from the left cerebellar hemisphere in 1941. In 1948 another tumor of the same type and location was removed, but it was impossible to decide from the operative findings whether a recurrence or a new tumor was present, and even though the first tumor was thought to have been radically removed, the case should perhaps best be classified as a recurrence.

LATE RESULTS

Of the 53 patients who survived the operation, 6 died later. One, as has already been mentioned, died as a result of removal of his second recu-

rence 4 years after the first operation. Three patients died some months up to 6 years after operation from intercurrent disease. In none of these cases was there any suspicion of recurrence. One patient died 11 years after operation with symptoms indicating a lesion of the brain stem, but ventriculograms 3 months before her death did not indicate the presence of an expanding lesion. She had been well and able to work for 10 years after operation. One patient died in his home 7 months after operation of "cerebral hemorrhage." Since the patient was only 45 years old and did not have hypertension, it seems possible that the cause of death might have been hemorrhage into a recurrent tumor.

Among the patients still living, 3 are invalids because of blindness, 1 because of cerebellar incoordination, and 1 because of mental impairment. The remaining 42 patients are well, although some of them may have some minor defects such as some impairment of vision. Because of the location of these tumors near the surface of the cerebellum, cerebellar incoordination is rarely a cause of disability, as it frequently is with more deeply situated tumors, such as the acoustic tumors.

SUMMARY

In a series of 4,101 verified brain tumors, 70 cases of cerebellar angioreticuloma were observed. In adults they occupy fourth place among the posterior fossa tumors, occurring with practically the same frequency as meningiomas, but less frequently than gliomas and neurinomas.

Cyst formation was found to be less frequent than generally thought, and almost one fifth of the tumors observed were entirely solid. In 5 cases, the tumor was located to the region of the fourth ventricle, in 9 to the vermis and in the remaining 56 to the cerebellar hemispheres. In 1 case von Hippel's disease of the retina was observed. Three families were observed where two or more members of the family were afflicted with angioreticulomas.

Among the symptoms, intracranial pressure is the most important and also the first symptom in most cases. Cerebellar symptoms were found in most cases, but were often late in appearance. Cranial nerve palsies, especially facial weakness and sensory disturbance in the trigeminal field, were observed in several cases.

Air studies were carried out in all but 3 cases. In cases of familial occurrence, vertebral angiograms are indicated, as multiple tumors are frequent in such cases.

Six patients died before operation. In 1 case the tumor was considered to be inoperable and decompression only was performed with an early fatality. In 63 cases the tumor was completely removed, with 10 fatalities. In 64 cases the mortality therefore was 17.2 per cent. Tumors located to the floor of the fourth ventricle carry a very high mortality, the operation having terminated fatally in 2 out of 5 such cases.

Among the survivors 6 died later from intercurrent disease. Five of the survivors are invalids, 3 because of blindness, 1 because of mental

impairment and 1 because of cerebellar incoordination. The remaining 4 patients are well and able to work.

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NEUROPHYSIOLOGICAL STUDIES ON CEREBRAL CONCUSSION*

R. B. AIRD, M.D., L. S. STRAIT, PH.D., D. ZEALEAR, M.D., AND M. HRENOFF, B.S.

Divisions of Neurology and Neurological Surgery and the Spectographic Laboratory of the University of California School of Medicine, San Francisco, California

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EXPERIMENTAL study of cerebral concussion and the post-concussional state has been greatly stimulated in recent years as a result of World War II and federal support of research projects along these and allied lines.[3] The mechanical effect of a concussive blow on the cranium has been clearly demonstrated by Pudenz and Shelden.[18] The transient increase in intracranial pressure and the neuronal discharge secondary to such concussive stimulation has been studied by Walker, Kollros and Case.[28] These and other studies indicate that the effects of mechanical factors are of paramount importance in the initiation of the changes associated with concussion. Such studies, however, do not explain the means by which the prolonged clinical and electroencephalographic effects of concussion† are produced.

Our own studies in this field,[3] aimed at this latter problem, have been stimulated by the concept that the maximal effect of a concussive blow might be expected in those areas where abrupt changes in the histological structure of the brain occur. Shearing forces are known to produce their greatest effect at such junction surfaces. Correspondingly, the major effects of concussion would not be expected to occur between cellular and extracellular elements, i.e., along the cell membranes of the relatively homogeneous cellular masses of the cerebral cortex. This concept is consistent with the effects of concussion on the semipermeable characteristics of the cell membranes observed by Spiegel, *et al.*,[21] who found that the permeability of the cortical tissue was only transiently altered by concussion and, therefore, would not appear to correspond with more prolonged post-concussional effects, such as cerebral dysrhythmia and the clinical findings. The same may be said of other transient neurophysiological changes, such as the alteration of acetylcholine metabolism after concussion (Bornstein[5]).

On the other hand, where the homogeneous cellular masses of the brain

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† The term "concussion" is used in its usual clinical sense and refers to a physiological disruption of neural activity without definite associated pathology. Windle *et al.*[31] and unpublished data from our laboratory,[26] however, have shown that slight histological changes can be demonstrated with cerebral concussion if more highly refined neuropathological techniques are employed. For a complete review of the subject of head trauma and especially for the gross alterations occurring in more severe injuries, the reader is referred to such authors as Spurling,[20,24] Evans,[10] and Matson.[17]

join other structures of different histological character, which are relatively large and fixed, such as the ependymal lining of the ventricular spaces and especially where the cellular masses of the brain make contact with their supporting cerebrovascular tree, one might expect greater shearing forces and neurophysiological changes. Such neurophysiological effects presumably would consist of changes in vascular permeability and associated transvascular alterations of a biochemical nature, which would affect cerebral metabolism. Depending upon its severity and duration, neurophysiological changes and even irreversible, degenerative changes might be produced. The perivascular pathology, described by Evans and Scheinker[11,12] and others, in more severe traumatic lesions of the brain, would be in keeping with this concept. Also, it would appear to be in keeping with the subependymal pathology and possibly the changes in the region of the falx and tentorium stressed by several authors (Spiegel,[22] Courville[7]) as being typical of cerebral concussion. The latter, in explanation of *contrecoup* injuries, suggests that pressure waves (or "force") may be transmitted directly through the brain with little or no ill effect, but produce relatively severe damage near the point of contact between brain and skull or other fixed structures, such as the falx and tentorium.

METHODS

As an index of the effect of concussion on the vascular structures of the brain, we have studied alterations of the semipermeable characteristics of the cerebrovascular system (blood-brain barrier). The technique involved determinations of the distribution of cocaine by spectrophotometric methods in the brain and blood following the intravenous administration of this drug in control and in traumatized groups of cats. The object of these experiments was to determine whether or not alterations in the concentration of cocaine occurred in the central nervous system following cerebral concussion, which might reflect permeability effects of possible neurophysiological and etiological importance in cerebral concussion and the post-traumatic head condition.

Animal Experimentation. In order to rule out transient neurophysiological effects of concussion (Spiegel,[21] Bornstein[5]) all post-traumatic experiments were conducted 3 days after cerebral concussion (technique described in previous report[3]).

Except for one series of studies (Table 2), all experiments were performed on individual cats as described below in contradistinction to the pooled specimens of 5 cats in each experiment as described in a previous study.[3] Special studies on the concentration of cocaine in blood (Table 2) were made with both methods (pooled specimens from 5 cats[3] and specimens from individual cats) in an effort to obtain more critical data on the crucial question of whether the concentration of cocaine in the blood was increased after cerebral concussion. In these studies the blood was taken together with specimens of liver (15 gm.) 15 minutes after completion of the intravenous injection of cocaine hydrochloride, but differed from the other experiments in that cerebrospinal fluid (cisternal puncture) and cortical specimens were not obtained prior to the collection of the blood.

The intravenous administration of cocaine hydrochloride (15 mg. per kg. of body weight of a 6 per cent solution) under chloralose and paraldehyde narcosis, and the collection of the cerebrospinal fluid (2–3 cc.), cortex (10–13 gm. obtained from both cerebral hemispheres and excluding diencephalon and white matter), and blood (25 cc. by direct cardiac puncture) specimens followed the technique described in a previous report,[4] except that the brain specimen was frozen in carbon-dioxide snow rather than liquid air.

The techniques of experimental concussion and electroencephalography were described in previous reports.[3,4] In connection with the EEG phase of the study, it should be emphasized that only cats that were normal from an EEG standpoint were selected for the studies. Likewise, only cats showing an abnormal EEG tracing following traumatization were used in the traumatic series.

Spectrochemical Studies. The specimens were analyzed for cocaine by means of chemical extraction and ultraviolet spectrophotometric measurements. A modified technique of extraction was developed, permitting the quantitative extraction and determination of as little as 0.1 mg. of cocaine in vitro from 12 gm. of brain, with 90 per cent recovery and an estimated error of the order of 10 per cent.[25] The spectrophotometric technique possesses the added advantage that spurious results due to contaminants can be minimized.

Absolute measurements in vivo are in error due to background contamination, but the consistency of data in repeated experiments has indicated that this source of error is essentially constant and has influenced the relative values only to a minor degree. In the present experiments the spectrophotometric measurements were made with a direct reading, photo-electric, ultra-violet spectrophotometer (Beckman), whereas the earlier studies[2,3] were made photographically with a Hilger, medium, quartz spectrograph and a Spekker photometer. Whereas the longer wave length absorption band of cocaine at 2750A alone could be measured conveniently with the spectrographic method, both bands characteristic of cocaine (2320A as well as 2750A) were readily measurable photo-electrically. Because the band at 2320A has an extinction coefficient approximately 12 times as great as the band at 2750A and the background absorption is increased only by a factor of the order of two, the proportional contribution of the background was appreciably reduced (approximately six-fold) in the measurements based on this band. The concentration of cocaine obtained from the measurements of the 2320A band are recorded because they have greater absolute accuracy; the values obtained using the 2750A band, however, gave the same *relative* results in all experiments.

Trypan Red Studies. Since in earlier studies[2] it was found possible to lower the permeability of the blood-brain barrier by intravenous injection of trypan red, it seemed desirable in the present study to use this mechanism to prevent, if possible, the increased permeability of the blood-brain barrier occasioned by cerebral concussion. In addition it was hoped that a relationship might be established between the altered permeability of the blood-brain barrier and the cerebral dysrhythmia associated with cerebral concussion. If the dye injections counteracted the effect of concussion on the permeability of the blood-brain barrier, they should also abolish the cerebral dysrhythmia providing the dysrhythmia was neurophysiologically related to, and dependent upon the altered blood-brain barrier effect.

With these objectives in mind, further series of experiments were performed after trypan red had been administered to cats, using as before both control and post-concussional animals. An intraperitoneal injection of 1.65 cc. of a 1 per cent

solution of trypan red per kg. of body weight was given. Four such injections were given over a period of from 5 to 7 days. The last injection of trypan red was given 5 days prior to the final cocaine experiment. The experiments in all other respects were identical with the experimental methods described above.

RESULTS

The results may be presented in two parts in accordance with the two distinct series of experiments performed in this study.

Part I. *Initial studies on the permeability of the blood-brain barrier in control and post-traumatic cats*

The basic data on the three-day post-traumatic cats, handled on an

TABLE 1

Spectrochemical determination of distribution of cocaine hydrochloride in the blood and brain of cats before and 3 days after traumatization*

Treatment	Cat #	Cocaine Level (gamma/gm.)	
		Blood	Brain
Control (no trauma)	43	5.3	28.4
	44	6.0	32.7
	45	9.4	33.6
	50	7.8	24.6
	53	4.9	26.7
	54	6.6	24.6
	57	—	25.3
	58	9.8	25.4
	60	6.3	33.9
	62	6.0	30.2
	66	5.9	28.0
	67	5.2	33.6
	70	4.7	33.4
	71	2.7	25.4
	72	8.4	28.5
	73	3.8	—
Three days after concussion	46	7.2	37.0
	47	5.8	33.4
	48	6.0	33.2
	49	7.7	39.6
	51	6.4	24.0
	52	7.8	36.3
	55	4.6	28.2
	56	5.7	33.3
	59	9.4	41.5
	61	5.2	44.0
	63	7.3	27.0
	64	6.6	33.9
	65	4.7	—
	68	5.2	33.7
	69	6.0	32.4

* Cocaine hydrochloride, 15 mg. per kg. of body weight, administered intravenously, as described in text.

individual basis, are shown in Table 1. These results are presented graphically in Fig. 1. The results of the special studies on the concentration of cocaine in blood, which were performed by two methods (pooled specimens

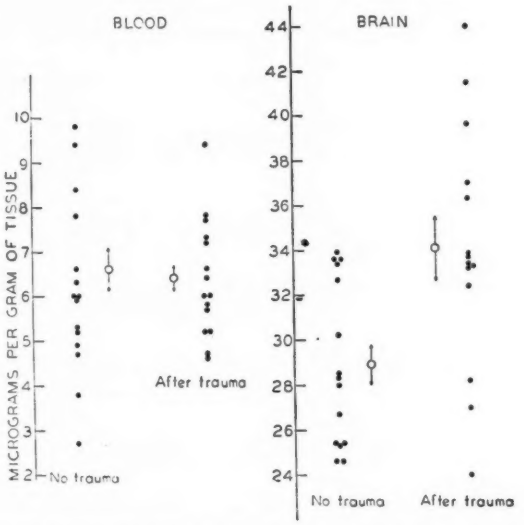

FIG. 1. Spot graphs showing the spread of experimental determinations, the mean values, and the standard deviations of the means on the distribution of cocaine hydrochloride in the blood and brain of cats before and 3 days after cerebral concussion.

from 5 cats as described in our previous report) and specimens from individual cats as described above under Methods) to obtain more critical data on the question of whether or not the concentration of cocaine in the blood was increased after cerebral concussion, are shown in Table 2.

The analysis of the data (Table 3) includes the mean values, the standard deviations of the mean values, and tests of the significance of the difference of the means. The latter are expressed in the last column in terms of the odds against the difference being due to chance.

The validity of the significance test depends in part upon the supposition that the values included in the analysis are representative samples, which follow the normal distribution law. The data, therefore, were subjected to a simple test capable of showing the nature of their statistical distribution. The approximation of the data to a straight line when plotted on probability paper indicated that they followed a normal distribution sufficiently close to warrant the statistical testing of their significance. In addition, Student's T distribution test gave results that were essentially the same as the standard deviation test for significance as shown in Table 3.

In the initial series of experiments in our previous study,[3] 8 control and

6 post-traumatic values appeared to show a significant rise in the concentration of cocaine in the blood after trauma as compared with the control values (see Tables 9 and 11 of the previous study[3]) which failed to show this same result. The apparently significant results in the initial series of experiments and the fact that the results in the more limited data of the second series of experiments, although not significant, were in the same direction

TABLE 2

Spectrochemical determination of cocaine hydrochloride in the blood† of cats before and 3 days after cerebral concussion*

Control (No Trauma)		3 days after Cerebral Concussion	
Experiment #	Cocaine Level (gamma/gm.)	Experiment #	Cocaine Level (gamma/gm.)
19‡	4.2	20‡	5.9
21	6.4	25	7.7
22	6.2	26	4.0
23	4.7	27	9.1
24	4.3	30	5.5
28	4.8	31	5.5
29	4.6	32	7.2
35	5.0	33	8.0
36	4.9	34	4.5
39	6.6	37	5.1
40	6.8	38	5.2
		41	4.8
		42	5.0

* Cocaine hydrochloride, 15 mg. per kg. of body weight, administered (intravenously) as described in text.

† Blood specimens were obtained together with liver specimens 15 minutes after completion of the intravenous injection of cocaine hydrochloride, but differed from the other experiments in that cerebrospinal fluid (cisternal puncture) and cortical specimens were not obtained at 5 and 10 minutes respectively, following the completion of the cocaine injection.

‡ Group experiments performed on pooled specimens from 5 cats in accordance with methods described in previous paper.[3]

led to the tentative conclusion that there was a real rise in the concentration of cocaine in the blood after cerebral concussion. The results in the present more extensive experiments verify the negative results of the second series of experiments. The failure to show a significant change in the concentration of cocaine in the blood in 3 series of experiments, involving 32 control and 34 post-traumatic values, as opposed to the apparent change of cocaine values in the initial series of experiments (8 control and 6 post-traumatic values) indicates that the concentration of cocaine in the blood is *not* altered by cerebral concussion.

The concentrations of cocaine in the brain were found in the earlier study[3] to be higher after trauma than in untraumatized control exper-

ments. The present studies (Table 1) are consistent in showing the same qualitative results. Considering all available data on the cerebral cortex involving 31 control and 26 post-traumatic values on the motor, occipital and whole cerebral cortex, it is clear that a rise in the concentration of cocaine occurs after cerebral concussion.

TABLE 3

Summary of statistical analysis of data on distribution of cocaine hydrochloride in the blood and brain of cats before and 3 days after traumatization*

Specimen	Treatment	Number of Experiments	Mean Value of Cocaine (gamma/gm.)	Standard Deviation	Significance Test	Odds†
Cerebral‡ cortex	Control (no trauma)	15	28.9	0.9		
	Traumatized	14	34.1	1.5	3.0	370:1
Blood‡	Control (no trauma)	15	6.6	0.5		
	Traumatized	15	6.4	0.3	0.3	<1:1
Blood§	Control (no trauma)	11	5.3	0.3		
	Traumatized	13	5.9	0.4	1.2	2:1

* Cocaine hydrochloride, 15 mg. per kg. of body weight, administered intravenously, as described in text.

† Odds against results being due to chance.

‡ Data from Table 1.

§ Data from Table 2.

The definite rise in the concentration of cocaine in the cortex after concussion in the presence of unaltered cocaine levels in the blood indicates a modification of the permeability of the blood-brain barrier after cerebral concussion. This is in agreement with the results of previous work in this field both by ourselves and others.

Electroencephalographic findings obtained in this study are in general agreement with those reported by other workers.[16] The greatest abnormality after mild or moderate cerebral concussion was observed in recordings obtained after a one-day interval in other studies.* The abnormality, however, persisted in a high percentage of cases for several days (83 per cent still definitely abnormal 3 days after concussion in this study), but was

* Unpublished data.

TABLE 4

Spectrochemical determination of cocaine hydrochloride in blood and brain of cats pretreated with trypan red,† before and 3 days after cerebral concussion*

Treatment	Experiment Number	Cocaine Level (gamma/gm.)	
		Blood	Brain
Trypan red (no trauma)	1	4.9	24.3
	2	7.9	28.5
	3	4.6	24.0
	4	—	20.4
	5	5.7	20.4
	10	8.6	28.6
	16	5.9	28.5
	17	5.1	25.0
	18	5.7	27.3
	19	6.9	32.3
Trypan red (3 days after concussion)	6	5.5	22.6
	7	6.1	17.6
	8	6.5	17.1
	9	5.2	16.5
	11	6.1	28.6
	12	4.9	25.4
	13	5.9	23.8
	14	6.5	19.7
	15	7.2	23.6

* Cocaine hydrochloride, 15 mg. per kg. of body weight, administered intravenously, as described in text.

† Trypan red, 1.65 cc. of a 1 per cent solution per kg. of body weight, injected intraperitoneally. Four such injections were given over a period of from 5 to 7 days.

TABLE 5

Summary of statistical analysis of data on distribution of cocaine hydrochloride in the blood and brain of cats (before and 3 days after cerebral concussion) after preliminary injections of trypan red†*

Specimen	Treatment	Number of Experiments	Mean Value of Cocaine (gamma/gm.)	Standard Deviation	Significance Test	Odds‡
Blood	Control (no trauma)	9	6.1	0.5	0.2	<1:1
	Traumatized	9	6.0	0.2		
Cerebral Cortex	Control (no trauma)	10	25.9	1.2	2.3	45:1
	Traumatized	9	21.7	1.4		

* Cocaine hydrochloride, 15 mg. per kg. of body weight, administered intravenously as described in text.

† Trypan red, 1.65 cc. of a 1 per cent solution per kg. of body weight, injected intraperitoneally. Four such injections were given over a period of from 5 to 7 days.

‡ Odds against results being due to chance.

found in a progressively smaller percentage of cases at longer intervals (20 per cent abnormal 1 week after concussion and 8 per cent abnormal 1 month after concussion in other studies).*

Part II. *Studies on the permeability of the blood-brain barrier following injections of trypan red in control and post-traumatic cats*

The results of these experiments are presented in Table 4. An analysis of the data is presented in Table 5 and the results are graphically shown in Fig. 2.

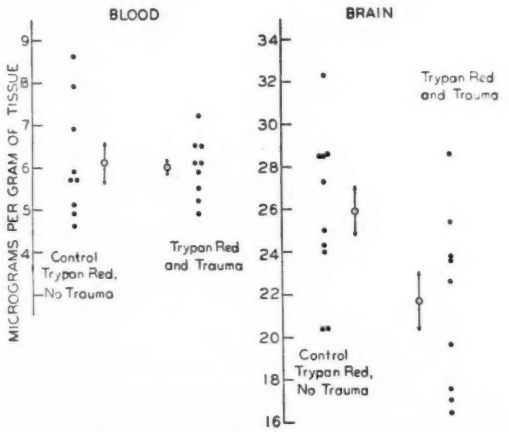

FIG. 2. Spot graphs showing the spread of experimental determinations, the mean values and the standard deviations of the means on the distribution of cocaine hydrochloride in the blood and brain of cats (before and 3 days after cerebral concussion) after preliminary injections of trypan red.

The results on blood after preliminary trypan red treatment, which involved 9 control and 9 post-traumatic determinations, agree with the previous observation that no change in the concentration of cocaine occurs in the blood after concussion. It is also of interest that the values for blood in this series of experiments are essentially the same as obtained in the previous series (Table 3) without trypan red. Inasmuch as the experimental methods were comparable in both series of experiments (except for the blood values of the special experiments, Table 2, in which cerebrospinal fluid and cortical specimens were not taken previous to the blood specimen), these results indicate that trypan red has no effect in altering the concentration of cocaine in the blood. They also further substantiate the previous observation that cerebral concussion does not alter the concentration of cocaine in the blood.

The data on the cerebral cortex after preliminary trypan red injections,

* Unpublished data.

which involved 10 control and 9 post-traumatic values, might be interpreted as indicating that the combination of trypan red and concussion produces a lowering of the concentration of cocaine in the cortex. These results (significance test of 2.3 and odds of 45 to 1, based on the assumption of a normal distribution of data), however, must remain somewhat uncertain. Regardless of this point, it is clear that a rise in the concentration of cocaine in the cortex does not occur after concussion providing the animal has received previous injections of trypan red.

A comparison of the post-concussional results in comparable experiments (Tables 3 and 5) shows even more strikingly that trypan red may effectively counteract the effect of cerebral concussion on the permeability of the blood-brain barrier. With blood values which did not significantly alter, the mean concentration of cocaine in the cortex after concussion and without trypan red rose to 34.1 ± 1.5 gamma per gm. of tissue, whereas the corresponding mean concentration of cocaine after concussion and after preliminary trypan red injections was 21.7 ± 1.4 gamma per gm. of tissue. An analysis of the post-concussional data, which involve 14 control values without trypan red and 9 determinations after preliminary injections of trypan red, gives a significance test of 6 and odds of 5×10^8 to 1 that these results are not due to chance. This striking result may be seen graphically by comparing the post-traumatic brain data of Figs. 1 and 2.

A corresponding comparison of the control values in these same experiments (Tables 3 and 5) is of interest in that these results may be compared with the values obtained in previous studies.[2] The initial studies on trypan red showed a significant decrease in the concentration of cocaine reaching the cortex after trypan red injections as compared with control experiments in which trypan red was not used. The present results are consistent in showing a shift in the same direction (lower concentrations of cocaine after trypan red therapy), although quantitatively the difference is less in the present studies than in the earlier report.[2] Increased experience with the experimental methods used in these studies, the collection of a larger volume of data, and the improvements in our technique (including the use of the 2320A band with the Beckman Spectrophotometer lead us to believe that the lower values obtained in the present experiments are more reliable than the values reported in the earlier studies.

Electroencephalographic Findings. A review of the EEG results suggests that the cerebral dysrhythmia observed after cerebral concussion in cats previously treated with trypan red is intermediate between the normal controls and the dysrhythmia found after concussion but without preliminary trypan red injections. In several experiments the EEGs after concussion (with trypan red) appeared normal and essentially identical with the EEGs obtained prior to concussion. In other experiments, a slight dysrhythmia appeared after concussion (with trypan red) but in general, as may be seen in Table 6, the EEG changes were relatively slight in the experiments with trypan red as compared with the experiments without trypan

red. Representative EEGs before and after concussion and with and without preliminary trypan red injections, are shown in Fig. 3.

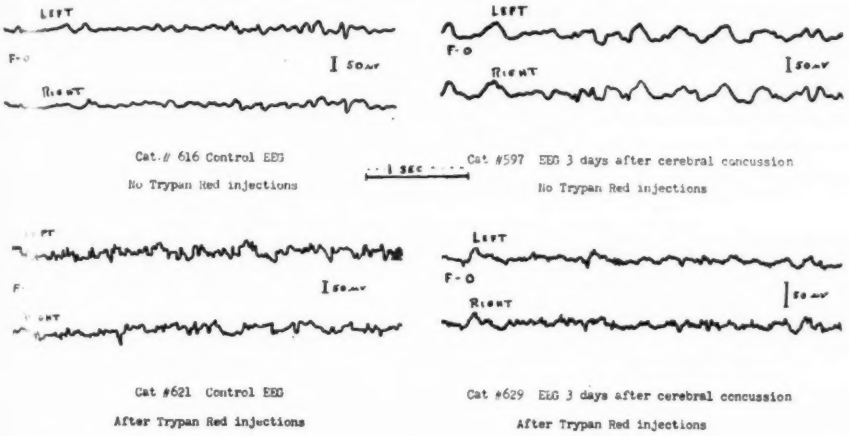

FIG. 3. Typical EEGs of cats before and after cerebral concussion and with and without preliminary trypan red injections (4 intraperitoneal injections of 1.65 cc. of a 1 per cent solution per kg. of body weight, over a period of 6 days, the last injection being 5 days before the final experiment).

DISCUSSION

Considerable neurophysiological evidence to which reference was made in an earlier study[3] suggests that the permeability of nerve tissue and of the blood-brain barrier is altered after cerebral concussion and that this may be associated with profound physiological changes and dysfunction even though neuropathological findings are slight or absent.

In summary, these experimental studies have suggested that cerebral injuries may produce three types of effects: (a) an alteration of the permeability of the entire blood-brain barrier after cerebral concussion, (b) a local modification of permeability and (c) a local modification of the reactivity of the nerve tissue focally injured. The present results, including thorough control studies, substantiate the effect of concussion upon the permeability of the blood-brain barrier and corroborate the suggestive findings of the earlier workers in this field. It seems clear, however, that we must differentiate between the effects of cerebral concussion and cerebral contusion associated with specific local pathology. The former is associated with an alteration of the permeability of the blood-brain barrier as proposed by other workers and as demonstrated in the present experiments. Furthermore, it is of interest, in this connection, that Spiegel[21] has shown that the permeability of the cerebral tissue is only transiently altered after cerebral concussion. On the other hand, there is reason to believe that the permeability and reactivity of cerebral tissue, altered pathologically, may well be increased and remain so altered over prolonged periods as suggested

by the studies mentioned.[8,19] It is not clear, however, what the role and status of the blood-brain barrier may be in the presence of cortical pathology after the initial and more generalized effects of cerebral concussion have worn off following cerebral contusion. Further investigation along these lines, although important and necessary, is not pertinent to our immediate studies on cerebral concussion.

In the present studies, blood determinations were made in all experiments as a necessary control, inasmuch as it is not justifiable to draw conclusions with respect to alterations of permeability without precise information as to the concentration of the agent on *both* sides of the tissue barrier concerned. This fact has been overlooked by many of the earlier investigators

TABLE 6

EEG findings in control and post-traumatic cats with and without preliminary trypan red injections†*

Experiment	Normal		Probable Normal		Probable Abnormal		Abnormal	
	No. cats	%	No. cats	%	No. cats	%	No. cats	%
Control*	82	78	23	22	0	0	0	0
Post-traumatic								
No trypan red	0	0	4	4	13	13	80	83
Trypan red†	6	67	1	11	1	11	1	11

* EEG data on control cats include results obtained in several experiments other than those reported in this paper.

† Trypan red, 1.65 cc. of a 1 per cent solution per kg. of body weight, injected intraperitoneally. Four such injections were given over a period of from 5 to 7 days.

who have assumed that the blood level remained constant in both their pre- and post-traumatic experiments. Consequently, the validity of much of the earlier experimental work in this field may properly be questioned. This may not be true of certain dye studies, however, inasmuch as it has been shown repeatedly that the central nervous system is normally impervious to wide variations of concentrations of acid dyes.

Again, in the field of cerebrovascular permeability studies apparently inconsistent results have been obtained, which in part at least may be explained by differences of technique and differences in the experimental conditions of the preparation being studied. Thus, in Broman's[6] supravital dye studies on brain injuries, a prompt "vascular lesion" of but short duration was obtained. As Broman comments, however, the sensitivity of the supravital dye technique for studying permeability may be "crude and that negative results obtained thereby do not exclude the possibility of a slight impairment of the permeability." Again, with respect to the condition of the preparation, Broman's brain injuries were associated with "punctate hemorrhages," and "multiple small hemorrhages." Considering this and the technique employed, Broman's explanation seems quite plausible that "The walls of the small vessels are probably ruptured with a consequenti l

immediate escape of blood cells. Later the vessels are either repaired or blocked by a total stasis preventing any further passage of the blood constituents (including the dye-stuff)." Such observations would appear to have little bearing on the present investigation concerned with concussion* in which an alkaline tracer substance, cocaine, which is relatively permeable for the central nervous system, has been utilized. Also, it should be emphasized that the present studies were conducted 3 days after concussion with the specific intent of ruling out transient effects such as those observed by Broman,[6] Spiegel,[21] and Bornstein.[5]

The variations of cocaine concentrations with respect to the time that the studies were conducted suggest that the rise is greatest in from 1 to 3 days after traumatization and in pooled specimens (technique used in initial study[3]) was not significantly altered at 1 week or later. These findings are of interest when compared with the electroencephalographic findings, which also showed maximal abnormality over this same period after concussion and which progressively became more nearly normal at 1 week and later following cerebral concussion. They also suggest that abnormal concentrations of cocaine might be found at later post-traumatic periods in those animals showing persistent abnormal EEGs. Since abnormal EEGs persisted in a relatively small percentage of the cats at later periods, it appeared unlikely that the group experiments, using pooled samples as employed in our initial studies on cerebral concussion,[3] could be used to show the delayed changes of the type found in the first 3 days after cerebral concussion. It was concluded that experiments on individual cats, which would enable a direct correlation with the EEG findings, were necessary to establish such a relationship. In part, it was for this reason that the present experiments were undertaken. The results of these experiments, although not performed at later intervals than 3 days after cerebral concussion, substantiate the findings of the initial experiments[3] and verify in the individual cat the prolonged association of the cerebral dysrhythmia and altered permeability of the blood-brain barrier after cerebral concussion.

The interesting possibility arises from these observations that this persistent phenomenon in the blood-brain barrier may correlate better with the dysrhythmia and clinical state seen after concussion than such transient alterations of neurophysiology as the increased permeability observed in cortical tissue by Spiegel,[21] or the findings of "free acetylcholine" for 48 hours after concussion† (Bornstein[5]). The correlation with such other observations as the water content of the brain,[33] the increase in brain volume,[30] the chromatolysis of the Nissl bodies,[15,32] and the appearance of nu-

* Not associated with hemorrhages or gross pathology, aside from the slight histological changes[26] as reported by Windle.[31]

† Acetylcholine in the cerebrospinal fluid over more prolonged periods as found by Tower and McEachern[27] would not appear to be comparable with the work of Bornstein[5] and the present studies on cerebral concussion, inasmuch as their observations were concerned with very severe cases of craniocerebral trauma in which subdural hematomas and intracerebral hemorrhage, requiring craniotomies, were demonstrated.

cleic acids in the cerebrospinal fluid[23] after cerebral concussion, as well as the effect of concussion on memory and capacity to learn, is even less definite. Although all these phenomena are presumably interrelated and essential manifestations of cerebral concussion, they would appear to be the effects of concussion rather than primary pathogenic mechanism in the production of concussion.

On the other hand, the demonstration of slight histological changes (Windle[31] and unpublished data from our own laboratory[26]) in cerebral concussion suggests that the neurophysiological effects of concussion diffusely involve the cellular elements of the brain. It is not clear, however, whether these changes are primary or secondary. It is conceivable for example, that some primary neurophysiological effect of concussion, such as an increased permeability of the blood-brain barrier, might so alter the biochemical environmental and metabolic processes of the cerebrum as to produce such slight histological changes.

Bornstein[5] in an experimental study of atropine therapy in cerebral concussion found that the cerebral dysrhythmia he observed electroencephalographically after concussion was modified and that atropine therapy also counteracted some of the clinical effects of concussion, such as stupor and loss of body tone. Considering the central stimulatory effect of atropine, the clinical effects of such therapy, perhaps, are not surprising. The "prevention" of the typical EEG effects of concussion (if the observed alteration of the EEG pattern by atropine can be so interpreted), however, are of great interest in view of our own results, which indicate that the supravital dye, trypan red, can abort the cerebral dysrhythmia as well as the increased permeability of the blood-brain barrier after cerebral concussion. The fact that acetylcholine, found by Bornstein[5] and Ward[29] in the cerebrospinal fluid after concussion, is a powerful vasodilator[14] suggests that this agent (even though its effect in concussion is transient and not necessarily the primary, pathogenic factor in concussion) might act to increase the permeability of the cerebrovascular tree. The anticholinergic effect of atropine in counteracting this might thus temporarily produce a result comparable to that observed with trypan red. If both atropine and trypan red tend to abolish the EEG effects of concussion, this would appear to be the most likely explanation of their similar or common action.

Since trypan red may prevent both the increased permeability of the blood-brain barrier and the cerebral dysrhythmia associated with concussion, it is of interest to evaluate the clinical significance of these experimental observations. The importance of this becomes obvious when it is realized that the possible relationship between these neurophysiological phenomena and the clinical symptoms seen after cerebral concussion cannot be established by experiment on animals. Trypan red, in that it can be used with safety in man, may aid in establishing or disproving such a relationship. If such a relationship can be established, it might be of considerable

importance in indicating therapeutic possibilities of clinical value in the post-concussional state.

Preliminary clinical studies, which are at present under way, suggest that trypan red and other agents[1] which have a corresponding effect on the blood-brain barrier may have some beneficial effects on the post-concussional state.

CONCLUSIONS

1. Neurophysiological studies, utilizing a modified spectrochemical technique for following the distribution of cocaine, have been performed on cats under control conditions and after cerebral concussion. The object of these experiments was to determine whether or not alterations in the concentration of cocaine occurred in the central nervous system following cerebral concussion, which might reflect permeability effects in the blood-brain barrier of possible etiologic significance in post-concussional head conditions. Significant rises in the concentration of cocaine were found in the cerebral cortex after concussion in agreement with our previous studies and the results of others. Although some data suggesting an alteration of the concentration of cocaine in the blood after concussion were presented in a preliminary report, this has not been confirmed in the completed study. The final data indicate that cerebral concussion increases the permeability of the blood-brain barrier, which substantiates the results of previous workers on this point.

2. Electroencephalographic studies indicated that approximately 80 per cent of the cats showed a cerebral dysrhythmia 3 days after cerebral concussion. The interesting possibility arises from these observations that these persistent post-concussional phenomena, e.g., the increased permeability of the blood-brain barrier and cerebral dysrhythmia, may correlate better with the clinical symptoms seen after concussion than the transient alteration of permeability observed in cortical tissue by Spiegel after concussion. The theory is advanced that the maximal effect of a concussive blow occurs at the point of contact between the cellular masses of the brain and such relatively fixed structures as the supporting vascular tree of the brain. It is postulated that disrupting effects at these points of contact might produce alterations of vascular permeability and secondary neurophysiologic changes affecting cerebral metabolism and that in more severe cerebral trauma perivascular pathology might be produced, resulting in irreversible changes of a degenerative character.

3. Similar studies following preliminary injections of trypan red showed concentrations of cocaine in the post-concussional cortex which were equal to or lower than the corresponding control values. No alteration of the concentrations of cocaine in the blood was observed after trauma when preliminary injections of trypan red had been administered. It was concluded that trypan red effectively counteracted the permeability effect of cerebral concussion on the blood-brain barrier.

4. After preliminary trypan red injections, the cerebral dysrhythmia recorded by electroencephalographic methods either failed to appear or appeared only in minor degree 3 days after traumatization. Since trypan red appears to counteract both the increase in permeability of the blood-brain barrier and the cerebral dysrhythmia associated with cerebral concussion, it may prove of practical value in determining the possible relationship between these neurophysiologic phenomena and the clinical symptoms characteristic of the post-concussional state. Inasmuch as trypan red may be used with safety in man, such therapeutic possibilities appear worthy of exploration. Preliminary clinical studies, which are at present under way, suggest that trypan red and other agents, which have a corresponding effect on the blood-brain barrier, may have some beneficial effect on the post-concussional state.

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LOCALIZED ENCEPHALITIS, BRAIN ABSCESS AND SUBDURAL EMPYEMA

1945–1950*

E. H. BOTTERELL, M.D., AND C. G. DRAKE, M.D.
Department of Surgery, University of Toronto, and the Neurosurgical Division of the Toronto General Hospital, Toronto, Ontario

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A REVOLUTIONARY change in the treatment of intracranial sepsis occurred during the second World War, when suppurating brain wounds were radically debrided by suction and closed without drainage. With the benefit first of the sulphonamides and later of penicillin primary healing occurred in a high percentage of cases.[2,21] This principle of primary closure of infected brain wounds was established by neurosurgeons at a time when delayed primary closure of war wounds of the extremities was mandatory. McKenzie,[16] in 1946, presented to the Toronto Academy of Medicine a study of 105 cases of brain abscess, treated over a period of 20 years at the Toronto General Hospital, with an overall mortality rate of 53.6 per cent. This trying experience was shared by all engaged in neurosurgery during the era before the use of antibiotics.

TABLE 1

Classification of intracranial sepsis
38 cases

1. Nonsuppurative localized encephalitis		5
2. Brain abscess		23
(a) Nonencapsulated	5	
(b) Encapsulated	18	
3. Acute diffuse subdural empyema		10
(a) *With brain abscess	4	
(b) Without brain abscess	6	
		38

* Included in consideration of acute brain abscess, nonencapsulated—III (a).

This paper presents an account of the methods and results of surgical treatment, supported by the antibiotics and sulphonamides, of a series of 38 consecutive cases of intracranial infection, during the 6-year period 1945 to 1950. On clinical and pathological evidence these cases were classified in three main groups (Table 1).

* Read before the Royal College of Surgeons of Canada at Montreal, December 1950.

I. DIAGNOSIS AND LOCALIZATION, IN GENERAL

Awareness of a potential primary focus of infection alerts the physician to the signs of increased intracranial pressure, such as headaches, drowsiness, vomiting and papilloedema, and to evidence of local disturbance of brain function—aphasia, hemiparesis, etc. It must again be emphasized that low-grade fever, a near normal white blood count and bradycardia are generally the common accompaniments of a brain abscess.

In recent years, valuable assistance has been obtained from the use of the electro-encephalogram in the recognition and localization of brain infection. X-rays of the skull may demonstrate gas in a brain abscess or displacement of a calcified pineal gland. A burr hole is made over the suspected site and the lesion is sought for with a brain needle. The resistance of the wall of an encapsulated abscess allows its ready differentiation from the soft, necrotic, nonencapsulated abscess. Occasionally accurate localization of an abscess is difficult. Cerebral angiography or ventriculography is then carried out.

II. ACUTE LOCALIZED NONSUPPURATIVE ENCEPHALITIS

Dandy[6] believed that "a hematogenous brain abscess passes through precisely the same stages of development that obtain for a furuncle." It is submitted that the inflammatory process following the spread of infection into the brain, regardless of its origin, runs a course similar to infection in other tissues. The inflammatory response begins with vascular congestion, oedema and cellular infiltration, resulting in a poorly localized nonsuppurative encephalitis. Before antibiotics and sulphonamides this process usually went on to suppuration, with the formation of a brain abscess, although in a few of these cases the process did resolve. McKenzie[15] in 1929 described three such cases under the heading of "Brain Abscess Suspect." Case 1 in our series illustrates the problem as it occurs today:

Case 1. A.C., a female, aged 50, was in good health until 4 weeks before admission when she visited her physician, complaining of nasal discharge. Ten days before admission a throbbing pain developed in the left ear, unassociated with any discharge. A week later general malaise developed, with headache, and on the day of admission she had four generalized convulsions. Following these her husband noticed that she was having difficulty with her speech. A lumbar puncture had been done; the CSF contained 160 cells/c.mm., chiefly polymorphonuclear leucocytes. The patient had received penicillin intramuscularly at home. She was admitted to the Toronto General Hospital as an emergency.

The patient was drowsy, with a temperature of 100° and a pulse rate of 70. She was dysphasic and had a right lower facial weakness. No field defect could be demonstrated. Early papilloedema was present in the left eye. The WBC was 13,500/c.mm.

An EEG showed high voltage slow waves from the left hemisphere, with phase reversals *localizing* the disturbance in the "central region near the fissures of Sylvius and Rolando on the left side." X-rays revealed clouding of the left mastoid antrum, as well as clouding of the left ethmoid and frontal sinuses.

She received large doses of penicillin, streptomycin and aureomycin. Her temperature returned to normal in 2 days and by the end of a week there were no neurological abnormalities. Three weeks after admission an EEG showed definite improvement. A pneumoencephalogram was done. There was no evidence of a space-occupying lesion. The left temporal horn was dilated as compared to the right. This was interpreted as atrophy of the temporal lobe following resolution of the inflammatory process. She remains well.

Case 1 was considered to be an example of early acute nonsuppurative encephalitis in the left temporal lobe. Four similar cases have been seen during the 6-year period. All 5 patients had one or more seizures and neurological signs of local disturbance of brain function, which were supported by electro-encephalographic studies. Treatment in the acute stage consisted of full doses of sulphadiazine, massive doses of penicillin and streptomycin, and more recently aureomycin. Close clinical supervision showed progressive recovery, in that the level of consciousness improved, focal signs such as dysphasia subsided and the temperature returned to normal over 2 or 3 days. This clinical course allowed us to defer special diagnostic measures. However, we regard it as most important to carry out air studies before a patient is discharged from hospital. This insures that a brain abscess has not formed and become quiescent under the intensive treatment with sulphonamides and antibiotics. Recovery has been uninterrupted for periods varying from 2 months to 3 years.

III. BRAIN ABSCESS

The primary sources of infection in this series have been, apart from trauma and operation, direct extension from the accessory nasal sinuses, middle ear or mastoid, and through the blood stream from pulmonary infection (Table 2).

When the infective process overwhelms the resistance of the brain and is uncontrolled by antibiotics, the inflammatory reaction proceeds to tissue death and suppuration. Commonly, the outcome is a well encapsulated abscess. On the other hand, a fulminating infection may result in suppurative softening of the brain without encapsulation. A ragged cavity filled with pus and softened necrotic brain may develop; a carbuncle may form. Surrounding the area of infection is a zone of cerebral swelling, which may spread to involve the whole brain at any stage in the development of an abscess. Successful management of a brain abscess requires surgical intervention before cerebral oedema and increasing intracranial pressure with tentorial and foramen magnum herniation develop to a fatal degree, regardless of the stage of maturity of the abscess and the development of a capsule. The most important clinical sign of the development of this serious irreversible situation is progressive deterioration of consciousness. Operative intervention should be undertaken *sufficiently early* to prevent intraventricular rupture of an abscess, with the development of ventriculitis and meningitis.

(a) *Acute Brain Abscess—Nonencapsulated.* Each of the 5 patients in this group, unassociated with subdural empyema, had reached the stage of rapidly deepening coma, due to cerebral oedema and increased intracranial pressure at the time of operation. The interval between the probable spread of infection to the brain and the development of coma was 3, 5, 7 and 7 days, and in one case of metastatic abscess the date of cerebral invasion was uncertain.

Case 2 illustrates the clinical course and surgical management of an acute nonencapsulated cerebellar abscess:

Case 2. F.O., aged 39. Since scarlet fever at the age of 2 the left ear had discharged intermittently. Three days before admission the discharge ceased and

TABLE 2

Etiology of abscesses in series 1945–50

	No. Cases	No. Deaths
Direct spread		
Otogenic		
Cerebral	7	1
Cerebellar	5	1
Paranasal sinusitis		
Frontal	4	
Frontal with subdural empyema	4	
Post-traumatic		
Compound anterior fossa fracture		
Frontal	2	1
Postoperative infection		
Frontal	2	
Metastatic		
Temporal	1	1
Occipital	1	
Parietal	1	
Total	27	4

headache and vomiting developed. He became progressively more drowsy and confused, and staggered as he walked.

On admission, his temperature was 100.4°, with a pulse rate of 56. There was purulent discharge from the left ear and X-rays showed evidence of chronic left mastoiditis. Signs of meningeal irritation, papilloedema, nystagmus, falling backwards and to the left, and ataxic movements of the left arm and leg pointed to the diagnosis of a left-sided cerebellar abscess. The neck was sufficiently stiff to suggest a purulent meningitis. A careful lumbar puncture showed an initial pressure of 230 mm. CSF; there were 190 cells/c.mm., with 75 per cent polymorphonuclear leucocytes.

On the evening of admission, 3 days after the onset of this illness, the lateral aspect of the left cerebellar hemisphere was explored. On opening the dura, soft,

semiliquid cerebellum under great pressure squirted into the field. Approximately the lateral third of the left cerebellar hemisphere was then sucked away, for it consisted of necrotic, softened cerebellar tissue and pus. There was no evidence of capsule formation. The pulse rate then rose to 100 and his respirations, which had become periodic under anaesthesia, resumed a normal rhythm. Penicillin (20,000 units) and streptomycin (50 mg.) were instilled into the abscess cavity. He had received 1,000,000 units of penicillin parenterally immediately before operation. The dura was closed tightly and the skin and muscle were closed in the usual fashion without drainage.

During the ensuing 4 days the patient received, daily, 20,000 units of penicillin and 50 mg. of streptomycin intrathecally, as well as 1,000,000 units of penicillin and 1 gm. of streptomycin systemically. The spinal fluid cell count fell rapidly and the patient was able to be up and about the ward on the 4th postoperative day.

One month postoperatively a left radical mastoidectomy was carried out, from which the patient made an uneventful recovery. At the time of discharge, neurological examination revealed only a minimal disturbance of balance and incoordination of the left arm. He has remained well for 1½ years.

TABLE 3

Brain abscess—nonencapsulated

No. Cases	Location	Treatment	No. Deaths
2	Cerebellar	Radical removal	0
1	Temporal	Radical removal	0
2	Temporoparietal	1. Aspiration	1
		2. Radical removal	0
4	Frontal		
	With subdural empyema	Radical removal	0
9	Total		1

Case 2 and those summarized in Table 3 are examples of acute brain abscess without encapsulation. All became surgical emergencies because of rapidly increasing coma. Aspiration fails to slacken off the brain, since the purulent, necrotic contents of the abscess are too thick to be evacuated through a brain needle. The unencapsulated abscess must be attacked in a radical fashion and sucked out completely, leaving viable tissue and a slack brain. Massive use of antibiotics systemically and in the abscess bed and where necessary, intrathecally and intraventricularly, has prevented the spread of infection.

The single death in this series occurred in an elderly pensioner with chronic lung abscess and empyema. He was moribund on transfer to the Toronto General Hospital and died shortly after aspiration of a deep left-sided temporoparietal abscess.

(b) *Brain Abscess—Encapsulated.* An encapsulated abscess is formed when the brain walls off the inflammatory process. This wall or capsule

consists of a layer of granulation tissue surrounded by a zone of proliferating fibroblasts and glial cells. The oedema may subside and the patient is temporarily released from the jeopardy of acutely spreading oedema and increasing intracranial pressure. This "walling off" of an abscess is what the neurosurgeon tried to wait for in the pre-antibiotic era, for at this stage the mortality following operation was reduced to about 25 per cent.[16] Usually there was enough pressure to prevent contamination of the subarachnoid space and drainage could be carried out safely. The abscess is a space-occupying lesion and gradually there will develop evidence of increasing intracranial pressure and, dependent upon the site of the abscess, signs of local disturbance of brain function. As in cases of nonencapsulated abscess, the terminal stage of spreading cerebral oedema with attendant coma may develop within a few hours and immediate evacuation of the abscess is required to save life. In like fashion, intraventricular rupture with the development of ventriculitis and meningitis requires operative elimination of the abscess.

Many other factors bear on the surgical treatment of an encapsulated abscess. It may be subcortical in situation or deep within the hemisphere. That area of the brain primarily concerned with speech or movement may overlie the abscess. Multiple or multiloculated abscesses are not uncommon, occurring in 5 of the 27 cases in this series. It follows that no uniform method of treatment is suitable for all cases.

The earlier cases of this series (1945–46) were treated, for the most part, by tube drainage or marsupialization (Cushing[5]) of the abscess capsule and drainage. Two patients in this early period were treated by radical removal of multiple encapsulated abscesses supported by the use of the antibiotics. The elimination of the septic process resulted in a shorter period of convalescence. As a result of this early experience and the then current reports of Pennybacker,[17] Cawthorne,[4] LeBeau[14] and Fincher[7] the method of radical removal of brain abscess was adopted wherever possible (Botterell[3]).

When a diagnosis of brain abscess has been established and the patient is neither comatose nor suffering from meningitis or rapidly advancing focal neurological signs, surgical treatment is largely guided by the situation of the abscess and the degree to which the capsule has developed. The abscess capsule is identified with a brain needle, the contents are aspirated and the pus is replaced with thorotrast, as described by Kahn,[12] and a solution containing 25,000 units of penicillin and 50 mg. of streptomycin. The size and exact position of the abscess are then established by X-rays. Bacteriological studies of the causative organisms are made to determine their sensitivity to the antibiotics. In some cases, if the position of the abscess is such that radical removal will result in severe neurological disability, an attempt is made to deal with it by multiple aspirations with the instillation of penicillin and streptomycin. This method of treatment seemed to be indicated in Case 3:

Case 3. L.C., aged 33. Three days after a left radical mastoidectomy there de-

veloped severe headaches and nominal dysphasia. Eight days after the operation an encapsulated left temporal lobe abscess was aspirated and thorotrast, penicillin and streptomycin were instilled into the cavity. Staphylococcus aureus was cultured from the pus. Three further aspirations were carried out at 3-week intervals, with instillation of penicillin.

Serial X-ray studies showed reduction in the size of the abscess from 2.5 by 1.5 cm. to 1.4 by 0.5 cm. No attempt was made to remove this abscess, for it lay in the left temporal lobe, intimately related to that area of the brain concerned with speech. It was considered that operative removal might convert a mild nominal dysphasia into a profound disturbance of speech. The patient has remained well for 3 years.

Of interest, concerning the rationale of this method, is Vollum's[24] report that penicillin and streptomycin are not inactivated by thorotrast. Greey[8] has found that thorotrast does not affect streptomycin over 24 hours at 37°C. Thorotrast inactivates 50 per cent of the added penicillin within 4 hours. There is no progressive destruction between 4 and 24 hours after exposure. It follows that one should err on the side of injecting large rather than small quantities of penicillin. Taylor[22] believes that many encapsulated abscesses can be dealt with successfully by repeated aspiration and instillation of antibiotics, and emphasizes the minor degree of surgical trauma as compared with excision. The method could not be generally applied in this series for the following reasons:

1. Many abscesses have sufficiently thick walls, when first tapped, that any rapid reduction in their size is not possible mechanically and they remain as a space-occupying lesion. Pennybacker[18] reports 2 cases in which the abscess enlarged in spite of repeated aspiration.

2. Not infrequently the abscess is multiloculated and only one cavity may be visualized in the X-ray, while one or more daughter abscesses may be present.

3. We believe that cerebellar abscesses, encapsulated and nonencapsulated, should be removed as a primary procedure because of the danger of irreversible damage to the brain stem.

In the early urgent case, it is therefore judged advisable to aspirate and visualize the abscess, filled with antibiotics and thorotrast, by X-ray. When the patient's condition allows, repeated aspirations are carried out until it is judged that the abscess has a capsule sufficiently thick to allow dissection. A period of 2 to 4 weeks is usually required. At that time the abscess is removed intact, if possible. Rupture through a thin portion of the capsule with contamination of the abscess bed or even the ventricle has not proved a serious matter, supporting the observations of LeBeau[14] and Pennybacker.[18]

In Case 4 the abscess was treated by repeated aspiration and removal:

Case 4. W.J., aged 50. An acute right frontal and ethmoidal sinusitis developed after a tooth extraction. Two months later he was admitted to the Toronto General Hospital with right frontal headache, confusion, vomiting and incontinence.

Neurological examination revealed only a confused mental state and bilateral papilloedema. The WBC was 11,000, temperature 99° and the pulse 52.

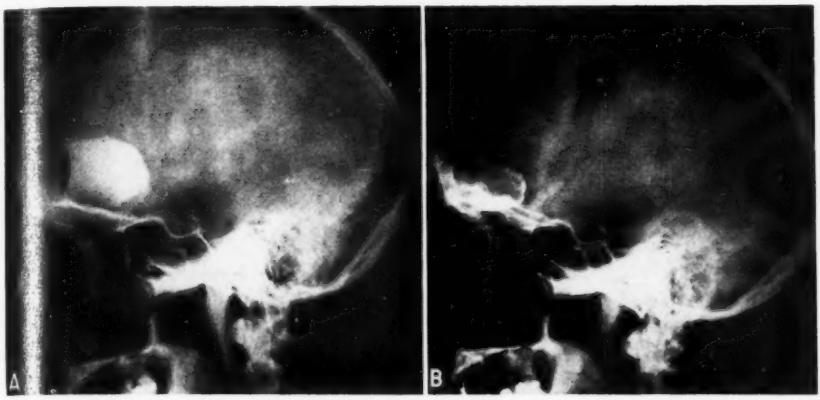


FIG. 1. *Case 4.* Lateral views. (A) Brow up, showing frontal lobe abscess filled with thorotrast immediately after first aspiration. (B) After 3 weeks: repeated aspirations. Note marked reduction in size of the abscess.

X-rays of the skull showed clouding of the right maxillary and frontal sinuses. The pineal was shifted to the left. An electro-encephalogram showed diffuse slow wave activity over the right hemisphere, although the changes were not sharply localized.

Two days after admission a right frontal abscess was aspirated through a right frontal burr hole and 30 cc. of thick yellow foul-smelling pus were obtained.

Penicillin, streptomycin and thorotrast were instilled into the cavity. This was followed by marked improvement in the patient's mental state. During the following 3 weeks the abscess was aspirated on three further occasions.

Progressive reduction in the size of the abscess was shown by serial X-rays (Fig. 1) and the patient became free of abnormal neurological signs and symptoms. At this time, through a small right frontal bone flap, the abscess was removed intact (Fig. 2). It was found to be adherent to the dura overlying the cribriform plate of the ethmoid.

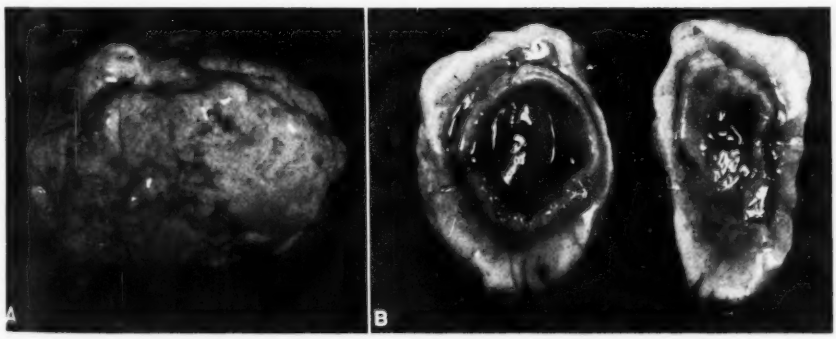


FIG. 2. *Case 4.* (A) Single abscess removed intact. (B) Cross-section of the abscess, showing thick capsule

The patient's course was uneventful and he was discharged well 11 days after the operation. At the time of discharge there was no evidence of active inflammation of the frontal or ethmoid sinuses. He has remained well for 2 years.

The treatment of the encapsulated brain abscess becomes an emergency when *coma has resulted from oedema and increased intracranial pressure.* Aspiration deals with the situation only when sufficient pus can be removed to relieve the pressure in the face of the generalized cerebral oedema, the space-occupying lesion persisting in the form of the abscess capsule, and possibly a second abscess. Successful reduction of intracranial pressure by aspiration converts the case from an emergency to an elective problem. This was done in Case 5:

Case 5. R.C., aged 14, began to have right frontal and temporal headaches, with stiffness of the neck, 3 weeks after a severe head cold. This was followed by persistent vomiting and 16 hours before admission he rapidly became semicomatose and was admitted as an emergency.

His temperature was 99.6° and his pulse was 52. There was bilateral papilloedema with a left VI nerve palsy. There were no other positive neurological findings. The WBC was 14,000 and skull X-rays showed clouding of the right frontal sinus.

Through a right frontal burr hole a large frontal lobe abscess was tapped and 3 oz. of pus were removed; 20,000 units of penicillin and 25 mg. of streptomycin with 3 cc. of thorotrast were injected into the abscess cavity. At this stage the brain was quite slack. A pure culture of Streptococcus haemolyticus was grown from the pus.

There was a rapid improvement in the level of consciousness. Four days later the abscess was aspirated again as his level of consciousness was deteriorating. There was no regression of the papilloedema, although he remained well and the abscess had decreased in size. One week later, following a negative aspiration, the abscess was removed intact. He received penicillin and streptomycin locally into the abscess bed and 1,000,000 units of penicillin intramuscularly daily.

Postoperatively, the patient did well and his papilloedema subsided rapidly. A spinal fluid leak through the nose closed spontaneously on the 5th postoperative day. He has remained well and has had no seizures.

In the event that coma is not relieved by aspiration of an abscess, radical removal must be undertaken as a life-saving measure. This was necessary in Case 6:

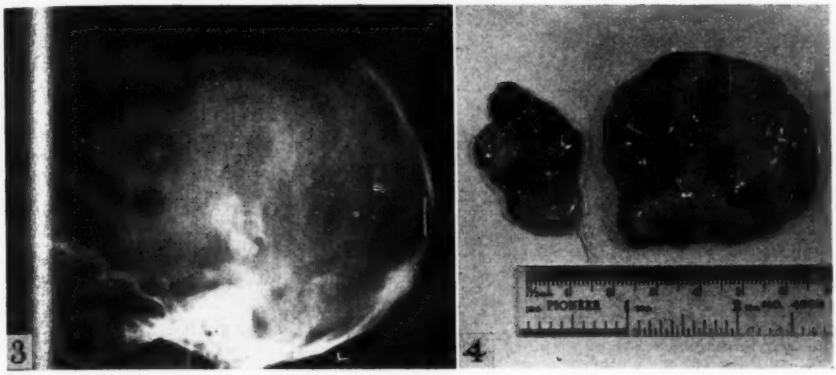
Case 6. A.G.,* aged 35, a pensioner, with bronchiectasis, was investigated neurosurgically because of headache and a single generalized convulsion 2 months prior to operation. With massive doses of antibiotics there was rapid clinical improvement. Ventriculography showed no clear evidence of a space-occupying lesion.

Ten days before operation severe headaches recurred and he became drowsy and confused. Bilateral papilloedema was the only positive neurological finding.

A few hours following a lumbar puncture he became unconscious, with a fixed, dilated, right pupil and periodic breathing. The WBC was 22,000. His pulse rate was 43.

* This patient was not operated upon at the Toronto General Hospital and is not included in the statistical studies.

Operation was undertaken when he was first seen. A right temporal lobe abscess was aspirated and 1 oz. of pus evacuated. Penicillin, streptomycin and thorotrast were instilled into the cavity (Fig. 3). The increased intracranial pressure was only partially relieved. There was little improvement in the patient's condition and 12 hours later the abscess was enucleated intact (Fig. 4). Streptococcus haemolyticus was grown in pure culture from the pus.



FIGS. 3 and 4. *Case 6.* (3) Lateral X-ray showing right temporal lobe abscess. (4) The overlying cortex (left) was removed and the abscess enucleated intact 12 hours later.

A stormy postoperative course followed, in which the patient was semicomatose for 2 weeks. He was given large doses of penicillin and streptomycin parenterally, and 15,000 units of penicillin daily intrathecally for 5 days. There was gradual improvement and 1 month after operation he was able to be up and about the ward, though still confused and slowed mentally. At discharge, there was a left-sided hemiparesis and a left visual field defect. The patient has continued to improve and there have been no seizures.

In retrospect, the patient in Case 6 would have been better treated by immediate excision of the abscess than by aspiration and later enucleation. There was a delay of 12 hours, between the time he was first seen and the abscess removed, with relief of the increased intracranial pressure and the hippocampal herniation. We believe this delay contributed to the severity and duration of postoperative semicoma and confusion.

Cerebellar abscess, even if encapsulated, by its position requires special consideration. The development of diffuse swelling of the cerebellum combined with acute internal hydrocephalus and transtentorial herniation, whether upward or downward, readily produces irreversible damage to the brain stem. Case 7 is illustrative and in addition bears upon the surgical treatment of Ménière's syndrome:

Case 7. C.F., aged 62, had onset of headache and staggering gait 2 years after electro-coagulation of the left labyrinth for Ménière's syndrome.

Two weeks later, when first seen, he was deeply unconscious, failing to respond

to the most painful stimuli. Breathing was stertorous and periodic. He was transferred to the Toronto General Hospital.

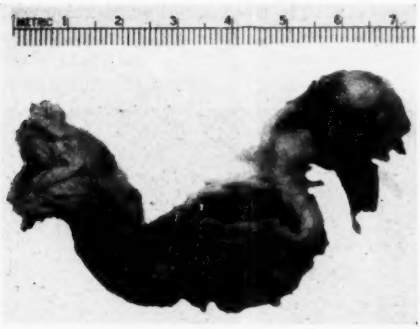


FIG. 5. *Case 7.* Chain of encapsulated abscesses removed from left cerebellar hemisphere.

Immediate operation was performed. No anaesthesia was necessary. The lateral aspect of the left cerebellar hemisphere was exposed. Pus was presenting on the surface of the cerebellum. With a brain needle an abscess capsule was palpated in the left cerebellar hemisphere. It was so dense that the brain needle could not be pushed through the capsule. A chain of brain abscesses was enucleated. A thick, tough stalk attached the mass to the dura overlying the postero-inferior surface of the petrous temporal bone (Fig. 5) in the region of the saccus endolymphaticus.

The patient did not rally and a ventricular tap showed that the brain was under no increase in pressure. He succumbed on the 4th postoperative day.

Case 7 is of two-fold interest. First, we are satisfied that these cerebellar abscesses represent deep spread of infection developing in mastoid and labyrinth after electro-coagulation for Ménière's syndrome. Secondly, there is illustrated the fact that removal of an abscess in the posterior fossa must be achieved before irreversible injury has been done to the brain stem.

Our overall experience with the clinical course of cerebellar abscess, especially following lumbar puncture, has emphasized how rapidly coma may develop, soon becoming irreversible. *We ourselves believe that the encapsulated cerebellar abscess, as well as the unencapsulated, should be excised as a primary procedure, using aspiration only for diagnosis and preliminary instillation of antibiotics.*

Surgical treatment is also an emergency when *spread of infection from an abscess occurs into the ventricle or the subarachnoid space.* Successful treatment of the ventriculitis and meningitis is impossible with recurring contamination from the abscess and radical removal is indicated. Recovery depends substantially upon the stage to which the ventriculitis and meningitis have progressed and upon the sensitivity of the infecting organism to the antibiotics. Pus may loculate in one lateral ventricle, due to occlusion of the foramen of Monro. Obstruction also occurs in the aqueduct of Sylvius or the foramina of the fourth ventricle. The problem is exemplified in Case 8:

Case 8. B.U., a 17-year-old boy, was admitted in a semicomatose state 5 months following an untreated compound depressed fracture of the right frontal bone. In the interval he had complained of headache and 2 days before admission a purulent meningitis developed.

Positive neurological signs were left lower facial weakness, bilateral upgoing toes and very marked opisthotonos. His temperature was 105° and WBC 20,000/c.mm.

Skull X-rays showed an old comminuted depressed fracture in the right frontal bone. Ventriculography done through a left frontal burr hole revealed a large space-occupying lesion in the right frontal lobe. The ventricular fluid was purulent, containing shreds of fibrin and many gram-positive cocci. Infection had spread from a deeply placed right frontal lobe abscess into the ventricle.

Through a right frontal bone flap a large right frontal lobe abscess was enucleated (Fig. 6). The communication with the ventricle was not definitely seen. On culture, the purulent ventricular fluid grew Staphylococcus aureus.

He was treated with large doses of penicillin, streptomycin and bacitracin intrathecally and intraventricularly. He received large doses of penicillin, streptomycin, aureomycin and sulphadiazine parenterally.

The patient survived for 8 days following operation. During that time his temperature returned to near normal and his spinal and ventricular fluid became clear. After initial improvement his clinical condition deteriorated and 3 days before death he became semicomatose and quadriplegic.

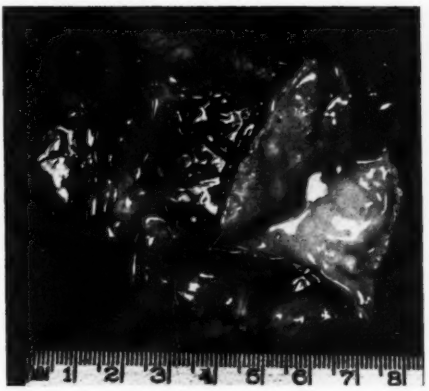


FIG. 6. *Case ..* The abscess, draining into the ventricle, has been removed. The exterior and interior of the capsule are shown. The communication with the ventricle was not found.

At autopsy the basal cisterns and the rest of the subarachnoid space showed no gross evidence of meningitis. A small amount of purulent exudate lay in the tips of both anterior horns of the lateral ventricles, the right anterior horn communicating with the operative defect. There was a small abscess cavity (8×6 mm.) lying in the genu of the corpus callosum which

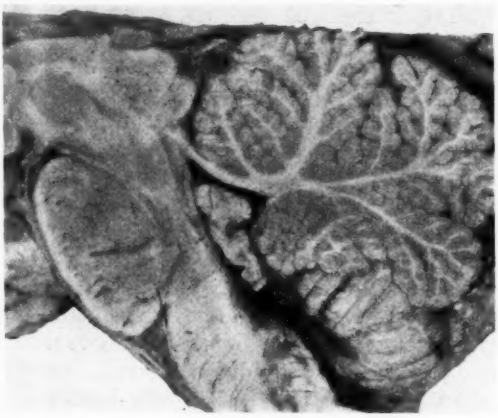


FIG. 7. *Case 8.* Sagittal section of brain stem shows fragment of of softened infected white matter occluding 4th ventricle.

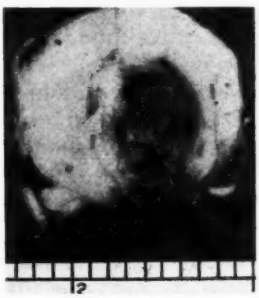


FIG. 8. *Case 8.* Cross-section of cervical spinal cord at approximately C6 shows extensive central haemorrhagic softening.

appeared to have ruptured posteriorly into the cavity of the septum pellucidum. Lying in the cavity of the 4th ventricle was a piece of softened infected white matter (Fig. 7). Although difficult to believe, it must represent white matter from the base of the operative defect in the right frontal lobe, which had passed through the 3rd ventricle and aqueduct to lodge in the cavity of the 4th ventricle. The lower end of the cervical enlargement of the spinal cord showed extensive central hemorrhagic softening (Fig. 8).

Case 8 is an outstanding example of an abscess following late upon an untreated compound depressed fracture with retained bone fragments in the brain and complicated by ventriculitis and meningitis. The abscess was removed and control of the infection in the lateral ventricles and the subarachnoid space was substantially achieved. Of great interest was the discovery that the fourth ventricle was filled by a plug of infected white matter and that hemorrhagic softening of the cervical spinal cord had occurred.

The methods of surgical treatment of the *encapsulated* abscesses, the incidence of multiple abscesses and the deaths are recorded in Table 4.

TABLE 4

Brain abscess—encapsulated

Treatment	No. Cases	Single	Multiple	No. Deaths
Total removal	10	6	4	2
Aspiration alone	1	1		0
Marsupialized	3	3		0
Tube drainage	2	2		0
Drained—later total removal	1		1	0
Negative exploration	1	1		1
Total	18	13	5	3

IV. SUBDURAL EMPYEMA

Acute diffuse subdural empyema commonly originates from acute inflammation of the frontal sinuses; less commonly the infection originates in the middle ear or mastoid. Deep spread from the sinuses to the subdural space is commonly accompanied by one or all of the following: subaponeurotic abscess, osteomyelitis of the skull, and extradural abscess. The infection may spread deeply again from the subdural space, causing meningitis and involving the brain with the formation of an abscess. Prior to the use of antibiotics and sulphonamides this disease was almost universally fatal.

During this 6-year period 10 patients with acute diffuse subdural empyema have been treated. In all save 3 cases the infection originated in the paranasal sinuses and of these 1 spread from an infected burr hole and 2 arose from infection in the mastoid (Table 5). The disease was bilateral in 3 of the 10 cases and in 4 patients acute nonencapsulated brain abscess had developed.

Diagnosis. The clinical picture is that of a drowsy or semicomatose patient, extremely ill, with high fever and leucocytosis, and signs of meningeal irritation. Fits are common and often commence in or are confined to the leg. Focal neurological signs may represent the effects of local pressure caused by pus pocketing in the subdural space, local cortical thrombophlebitis or the development of a brain abscess. Of particular interest was the presence of a visual field defect in 3 of the 10 patients. This affords a marked contrast to the rarity of a field defect in subdural hematoma. The explanation of this is based on the parasagittal spread of pus along the falx and involvement of the visual cortex.

TABLE 5

Subdural empyema

Source		Unilateral	7
Pansinusitis	7		
Otogenic	2	Bilateral	3
Infected wound	1		
No. cases	10	Associated with brain abscess	4
Deaths	0		

Treatment. Successful treatment, we believe, requires a planned surgical attack based on the following principles:

(*a*) *Adequate exposure and removal of subdural pus.* This requires an understanding of the directions in which the infection may spread. From the frontal and ethmoid sinuses, the spread is in three directions: *deeply* under the orbital surface of the frontal lobe and along the Sylvian fissure, *medially* along the falx ultimately to overlie the tentorium and *superolaterally* over the convexity of the hemisphere. Fig. 9 illustrates these pathways. Ray and Parsons[19] concluded from postmortem studies that subdural infection spreads to the opposite side under the falx cerebri.

A paramedian burr hole is made immediately above each frontal sinus. If no pus is encountered, more laterally placed frontotemporal burr holes are made as well as occipital burr holes. When subdural pus is encountered in the frontal region, the frontal sinus is completely removed, thus eradicating the primary focus and enlarging the dural exposure. A paramedian channel of bone about 2 cm. wide is removed for a short distance posteriorly, and as much additional frontal bone as may be judged necessary. The dura is opened widely to allow satisfactory examination of the parasagittal region, the convexity of the hemisphere and the orbital surface of the frontal lobe to the anterior Sylvian region. As much pus as possible is evacuated by suction.

(*b*) *Removal of complicating brain abscess, if present.* The region of the frontal pole is carefully examined for the presence of an acute nonencapsu-

lated abscess. Should an abscess be encountered, it is radically removed by suction.

(*c*) *Eradication of the primary source of infection.* As has been mentioned, the frontal sinus is removed to provide adequate exposure as well as to eliminate the primary focus. In the case of the mastoid, it is opened from above and the frankly purulent material removed. Definitive elimination of the mastoid as a source of infection is carried out by the otolaryngological service when the intracranial emergency has passed.

(*d*) *Adequate use of antibiotics.* Tubes for the local instillation of penicillin and streptomycin into the subdural space are placed along the falx,

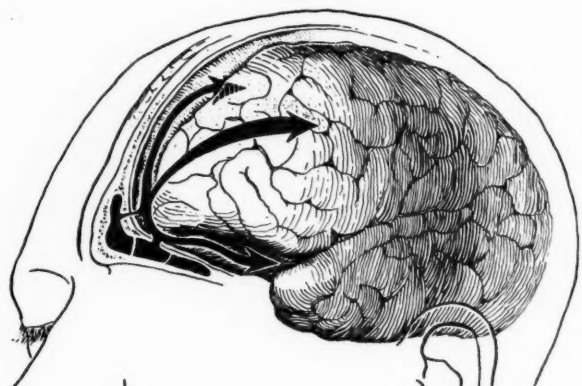


FIG. 9. The drawing shows the three directions of spread of the inflammatory process in the subdural space from the frontal sinus.

under the frontal lobe and over the hemisphere. The scalp is tightly closed around the tubes. Along with this local therapy, intrathecal penicillin has been used in some of the cases. All patients have received massive doses of the antibiotics systemically. In the future, with adequate levels of systemically administered antibiotics gaining access to the subdural space, the use of tubes for local instillation may be unnecessary. In our cases the tubes have not drained pus from the subdural space.

Case 9 illustrates many of the problems that may be encountered in treatment of a patient with acute diffuse bilateral subdural empyema:

Case 9. R.W., aged 19. Suppuration left frontal sinus; subaponeurotic abscess; osteomyelitis of the frontal bone; extradural abscess; bilateral subdural empyema; brain abscess.

Fourteen days after the development of a severe head cold this patient was admitted to another hospital with a temperature of 103° and an acute suppurative

left frontal sinusitis. He was confused and drowsy, with diplopia and signs of meningeal irritation. The frontal and ethmoid sinuses were cloudy by X-ray. The spinal fluid pressure was 350 mm. of water. There were 280 cells, 80 per cent of which were lymphocytes.

On the 17th day drainage of the left frontal sinus was carried out below the orbital margin and 1 oz. of pus evacuated. Staphylococcus aureus haemolyticus was cultured. On the 19th day a more radical frontal sinus operation was performed. A considerable amount of extradural pus was found. At this stage the patient was transferred to the Toronto General Hospital, 6 March 1950.

On admission, the patient was drowsy with temperature 104° and pulse 54. He appeared desperately ill. Pus was discharging from a left supero-orbital incision. There was a red, oedematous swelling of the frontal area. He was markedly dysphasic, and had a right-sided hemiparesis and homonymous field defect. Treatment with sulphadiazine, penicillin, streptomycin and aureomycin was immediately started.

Under general anaesthesia, 2 hours after admission, the whole frontal bone was exposed through a left frontal scalp flap. Acute osteomyelitis involved the central portion of the frontal bone. The infected bone, including the frontal sinuses and the anterior portion of the left orbital plate, was removed until normal bleeding bone was encountered. The frontal sinuses both contained thick pus. Beads of pus were seen escaping through the dura over both frontal poles. On opening the dura on the left side, subdural pus was encountered over the hemisphere, and evacuated. Further exploration revealed collections of pus along the falx and under the orbital surface of the frontal lobe. The frontal pole was occupied by an acute brain abscess, which was sucked out. Another collection of pus was evacuated from the region of the Sylvian fissure on the left side. A burr hole placed above the left ear showed that the pus did not extend back to this region.

On the right side only a thin layer of subdural pus was encountered, surrounding the frontal pole. Small catheters were then placed along the falx, over the lateral aspect and beneath the orbital surface of the frontal lobe on both sides, six catheters being used in all. These were brought out in groups of three through two small stab wounds in the scalp. The scalp flap was then tightly closed with a single layer of interrupted silk.

Postoperatively the antibiotics were continued by systemic and intrathecal routes, and penicillin and streptomycin were injected daily into each of the catheters. For the first 4 days the patient improved. However, 6 days after the first operation his level of consciousness was deteriorating, and the dysphasia and hemiparesis had returned.

A right posteroparietal burr hole was negative. An occipital burr hole on the left encountered subdural pus over the tentorium, along the falx and over the vertex, capping the occipital lobe. Catheters were again placed in three directions and the wound was tightly closed. The left frontal wound was reopened and a large recurrent left frontal abscess was found. This was again radically sucked out and a tube was placed in the abscess cavity and brought out through a stab incision. Penicillin and streptomycin were injected daily into the catheters around the occipital lobe and into the frontal abscess cavity.

The patient's recovery from this point forward was remarkable. The tubes were removed on the 3rd postoperative day and the patient was allowed to be up and about after the 5th postoperative day. Aside from an acute right-sided parotitis,

which quickly responded to X-ray therapy, further convalescence was uneventful. Apart from five generalized seizures, he has remained well for $1\frac{1}{2}$ years.

Results of Treatment of Subdural Empyema. There have been no deaths among these 10 patients. One patient is permanently hemiplegic and epilepsy has developed in 3 of the 4 patients with associated brain abscess. One patient has not been followed recently. Keith[13] reported 7 cases, 1 of which was the first of this series, without a death. Schiller, Cairns and Russell[20] recorded 3 deaths among 10 patients with subdural empyema. Gurdjian and Webster[9,10] had no deaths in 4 cases.

TABLE 6

Brain abscess—mortality

No. Cases		No. Deaths
9	Nonencapsulated (4 with subdural empyema)	1
18	Encapsulated	3
27	Total	4

TABLE 7

Analysis of deaths

1 Temporal lobe—unrecognized.

1 Multiple cerebellar abscesses—moribund—enucleation without anaesthesia.

1 Untreated compound depressed fracture; 5 months later admission with advanced ventriculitis and meningitis—radical removal—death from necrosis of spinal cord and occlusion of 4th ventricle by infected white matter.

1 Left temporoparietal—nonencapsulated metastatic—moribund—aspiration only.

DISCUSSION

Before sulphonamides and antibiotics, fear of spread of infection to subarachnoid or subdural space led to deferring drainage of an abscess until it was judged that a capsule had formed. In the face of multiple abscesses drainage was commonly inadequate and followed by cerebral herniation, meningitis or rupture into the ventricles with ensuing ventriculitis. With the antibiotics, widespread infection is no longer common and radical removal of encapsulated or nonencapsulated abscess may be undertaken as dictated by the clinical manifestations of increased intracranial pressure with brain stem compression by tentorial and cerebellar herniation.

Table 6 shows the overall mortality in our series of patients with brain abscess treated during the years 1945 to 1950, inclusive.

In Table 7 the deaths are analyzed briefly.

In no instance was the spread of infection following operation a problem, although in many cases the lateral ventricle was opened and contaminated during excision of an abscess as were the subarachnoid and subdural spaces. Attention has been called formerly to unilateral hydrocephalus resulting from obstruction of the foramen of Monro, and causing progressively deepening stupor and hemiparesis.[1]

Emphasis has been laid upon the advance in surgical therapy of brain abscess made possible by the antibiotics but equal emphasis must be laid upon the need for continued practice of sound surgery. The administration of penicillin does not substitute for the removal of retained bone fragments in a brain wound (Case 8) or for appropriate surgical treatment of an infected mastoid or frontal sinus. Watchful waiting, sheltered behind the administration of antibiotics, of a patient steadily becoming more unconscious from brain abscess is unjustifiable.

We believe that acute diffuse subdural empyema is but part of a widespread infection: an important part because pus pockets in the subdural space in sufficient quantities to cause death. While surgical treatment includes evacuation of pus and brain abscess if present, it remains for antibiotic therapy to control infection.

SUMMARY AND CONCLUSIONS

1. Resolution of early brain infection—"acute localized nonsuppurative encephalitis"—has been observed in 5 cases following treatment with the antibiotics and sulphonamides. This outcome of brain infection has become more frequent.

2. Radical removal of "nonencapsulated brain abscess" has been carried out by suction in the face of developing coma. Five cases are reported with 1 death; in 4 additional cases, complicating subdural empyema, the patients were similarly treated and survived.

3. (a) Encapsulated brain abscess—supratentorial—uncomplicated by coma, meningitis or ventriculitis, is best treated by repeated aspiration using thorotrast and instilling antibiotics followed by enucleation of single or multiple abscesses. Removal of the abscess is omitted where serious neurological deficit may accrue, e.g., dysphasia, hemiplegia, providing the patient remains well.

(b) Failure to "slack off" the brain and relieve coma by aspiration requires that radical excision should be undertaken at once.

(c) A cerebellar abscess should be removed immediately following verification by aspiration.

(d) Spread of infection into the ventricles or the subarachnoid space requires primary extirpation.

4. The antibiotics and, in lesser measure, the sulphonamides, control and prevent the spread of intracranial infection, making possible radical and effective surgical treatment of brain abscess with and without capsule formation.

5. Four deaths occurred in 27 cases of brain abscess treated during the 6-year period, 1945 to 1950. This group included 5 cases of multiple abscesses, 3 cases of metastatic abscesses and 4 complicated by subdural empyema.

6. Subdural empyema. A plan of treatment is presented. This is based on consideration of the directions of spread of subdural infection, removal of primary source of infection and adequate local and systemic antibiotic therapy.

Ten patients have been treated, 4 with associated acute frontal lobe abscess, without a fatality.

We wish to express our appreciation to Dr. Kenneth G. McKenzie for many helpful suggestions, both in the treatment of these patients and the preparation of this paper.

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TRIGEMINAL NEURALGIA

A REVIEW OF SIX HUNDRED AND EIGHTY-NINE CASES WITH A FOLLOW-UP STUDY ON SIXTY-FIVE PER CENT OF THE GROUP*

MAX M. PEET, M.D.,† AND RICHARD C. SCHNEIDER, M.D.

Section of Neurosurgery, Department of Surgery, University Hospital, Ann Arbor, Michigan

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TRIGEMINAL neuralgia may be treated with gratifying results by rhizotomy or its symptoms may frequently be relieved temporarily by alcohol injection of the divisions of the Gasserian ganglion. Usually any surgical therapy directed toward the relief of pain is accomplished only at the expense of a minor degree of new neurologic deficit, and that is particularly true in this condition. Success depends not only on the technical ability of the surgeon, but also on an understanding referring physician and a properly enlightened patient. Preoperatively all should have a clear insight into the postoperative problems that may confront the patient, such as crawling or burning paresthesias, numbness, and the possibility of corneal anesthesia and its dangers. There are numerous articles in the trigeminal neuralgia literature written by competent observers but no *complete* follow-up reports on any large series of cases have been found. In most instances there is a tendency to recall vaguely the number of patients who have been relieved of their tic pain or remember a low mortality rate, but actual percentages of unpleasant postoperative sensations sustained by the patient are too frequently omitted.

The vast majority of patients with typical trigeminal neuralgia will accept these sensations and be extremely grateful for the relief of their sharp knife-like tic pain, provided they have been forewarned.

In this paper we wish to present the data on 689 cases of trigeminal neuralgia which were examined at the University Hospital during the 10-year period from January 1, 1938, to January 1, 1948: (I) 553 patients had a trigeminal rhizotomy; (II) 49 individuals had only alcohol injections; and (III) 87 were diagnosed as having trigeminal neuralgia, but no procedure, either rhizotomy or injection, was performed.

A follow-up questionnaire was sent to all of these patients, and we were gratified to have 65 per cent of them reply. We regard this as an excellent response for patients having a lesion that characteristically occurs most frequently in the older age groups.

In a statistical survey of this magnitude it is impractical to attempt to

* This study was begun in January 1948, and was approximately half completed at the time of the death of the senior author in March 1949. Dr. Peet had reviewed the work and made several suggestions and corrections just preceding this date. The material was then laid aside for a period of two years at which time Dr. Edgar A. Kahn encouraged completion of the study.

† Deceased March 25, 1949.

compare the many figures of this study with data found in reviews of the topic by other neurological surgeons. For comparative analyses the reader is therefore referred to the comprehensive articles by Adson,[1] Coleman, Meredith and Troland,[2] Cushing,[3] Davis and Naffziger,[4] Frazier and Russell,[5] Harris,[6] Horrax and Poppen,[7] and Kirschner.[8]

Age. In our series of 689 cases, 74 per cent of the patients were over 50 years of age at the time of the initial examination; 34 per cent were over 65 years of age; and 10 per cent were over 75. In the group over 80 years, there was a total of 28 individuals. The youngest patient was 15 years and the oldest, 91. However, the 2 youngest, 15 and 19 years, respectively, were found at operation to have the fibers of the Gasserian ganglion matted together, suggesting an inflammatory process as the etiology for their pain. The youngest patient in whom the ganglion appeared normal was 21.

Sex Incidence. There was a 4:3 ratio of involvement in the female compared to the male.

Side of Involvement. The right side was involved more frequently than the left in a ratio of 8:5. At the time of the original examination 2.7 per cent of the patients had bilateral tic pain, but when the follow-up study was included, the incidence of bilateral involvement rose to 5.9 per cent. This figure is important in emphasizing that a patient may eventually require a bilateral rhizotomy, and therefore the motor root should be carefully identified and spared at each operation. Bilateral paralysis of the muscles of mastication supplied by the trigeminal nerve would cause the distressing problem of inability to close the mouth.

Duration of Symptoms. Slightly more than 17 per cent of the patients had had their tic pain for a period of over 10 years, 9.2 per cent had had their complaints for 15 years, and 4.7 per cent had had their difficulty for over 20 years. The lives of some of these patients were completely warped by their illness, for 8 had had the agonizing pain over a span of 30 years and a single patient had suffered for 40 years before coming to rhizotomy.

Division Involved.

Ophthalmic involvement alone	3.4%	24 cases
Maxillary involvement alone	16.5%	114 cases
Mandibular involvement alone	15.8%	109 cases
Ophthalmic and maxillary combined	13.9%	96 cases
Maxillary and mandibular combined	37.3%	257 cases
All three divisions combined	12.7%	88 cases
Ophthalmic and mandibular combined	0.1%	1 case

On summary, the ophthalmic division was involved in a total of 30.1 per cent of all cases, the maxillary in 80.4 per cent, and the mandibular in 65.9 per cent. Thus differential section with sparing of the ophthalmic division could have been attempted in 70 per cent of all the cases.

Trigger Zone. From the available data, 218 patients, or 31.6 per cent, had one or more trigger zones. The commonest sites were: the upper lip—52, ala nasae—42, angle of the mouth—30, nasolabial fold—22, lower lip—21, malar eminence—18, lower jaw—14. Only 17, or 2.4 per cent, of all the patients, had a trigger zone limited to the ophthalmic division. In 2 cases

the lobe of the ear seemed to be the trigger mechanism. From our experience we would be inclined to feel that more people had a trigger point than has been recorded above.

I. TRIGEMINAL RHIZOTOMIES

Preoperative Problems. Preoperative problems, not related to trigeminal neuralgia, were present in many cases. In most instances these were related to the older age group in which trigeminal neuralgia is prone to occur. In a few cases aggravation of these conditions was the cause of death. By far the greatest number of complications was associated with heart and kidney disease. There were 182 patients, 26 per cent, who were known to have hypertension, and another 41 patients were listed as having organic heart disease. Arteriosclerosis was sufficiently severe in 34 cases to make special note of it. Preoperatively hemiplegia was present in 6 individuals.

Inflammatory lesions such as syphilis were noted in 13 patients, multiple sclerosis in 8, and tuberculosis in 4. Diabetes presented a problem in 6 individuals. Deafness was present in 15 cases, blindness in 3, facial tic in 2, a 3rd nerve palsy in 1 and a 6th nerve lesion in another. In the latter two instances one would have suspected the presence of an aneurysm or tumor but none was demonstrated at operation through the lateral approach.

There were 24 patients who complained preoperatively of considerable loss in weight from inability to eat because of severe tic pain. This loss varied from 15 pounds within 2 or 3 weeks to 60 pounds over a period of $1\frac{1}{2}$ years. One patient, 84 years of age, lost 30 pounds so that her preoperative weight was only 78 pounds. Another patient stated that she had been on a liquid diet for 9 months and was unable to eat even semisolid foods. Starvation is an important problem which should be dealt with preoperatively if some of the older aged patients are to have a satisfactory postoperative course. Some neurological surgeons believe that one of the benefits of alcohol injections is transient relief of pain enabling the patient to eat and permitting development of a better physiologic balance preoperatively.

Operations. Fourteen surgeons performed the 553 trigeminal rhizotomies. The senior author operated upon 53.5 per cent of the patients. The remainder were treated surgically by other members of the permanent and resident staffs.

Preoperatively the patients were well sedated with morphine and scopolamine. All operations by the temporal approach were performed in the upright or sitting position, but the few suboccipital craniotomies were done in the prone position. Local metycaine or procaine infiltration anesthesia was used in 534 cases or 96.5 per cent. In only 1 instance was $1\frac{1}{2}$ per cent cocaine employed. Eighteen patients had general anesthesia. Frazier's temporal approach was used in 544 cases, and in only 9 cases was Dandy's posterior fossa operation employed. In 7 of the latter procedures both the 5th and 9th nerves were sectioned. In only 2 instances was this approach used for trigeminal rhizotomy alone.

Immediate Complications. One of the most interesting aspects of this

study was an evaluation of the problems encountered at the operating table. Since the upright or sitting position was employed almost exclusively, vasopressor agents had to be used or antigravity measures occasionally had to be taken to combat a drop in blood pressure. In 25 cases there was a sudden pronounced hypotension with pressures reaching shock levels or being unobtainable so that cerebrovascular accidents occurred in 7 patients. One of these individuals had had a moderate hypertension preoperatively and died on the table. It should be noted that during the past few years since this study local infiltration anesthesia has been supplemented with intravenous sodium pentothal, and not as much hypotension has been observed. In this way pain and fear stimuli are abolished and there is less tendency for shock to occur. These are important factors in an emotionally labile individual.

The development of hypertension during operation was a problem in 4 patients, and 1 of these had a cerebrovascular accident. In another of this group the elevation of blood pressure occurred when the suboccipital approach was used and the 9th nerve sectioned.

The next most common problem was a tendency of the sensory root to be matted together so that the divisions could not be readily dissected out and identified. This occurred in 23 patients. Three ganglia were described as being unduly large, two or three times normal size. Another ganglion was yellow in color and the operator suggested the possibility of hemosiderosis from a leaking aneurysm or multiple sclerosis, but there was no clinical evidence to substantiate either diagnosis. In 1 case the Gasserian ganglion was never identified.

The dura was markedly adherent in 11 cases, and in 1 of these cases firmly calcified plaques, which were imbedded in the dura, hindered the operator's progress. Heterotopic protrusions of the dura extending through the skull markedly hampered the exposure in another case.

Bleeding was troublesome in 7 patients. In 1 the diploë were extremely large and bled profusely. In 2 the cavernous sinus was a problem due to the marked adherence of the roots to its lateral wall; upon attempting to free them the sinus was entered, with marked hemorrhage resulting. In 1 patient there was profuse bleeding from an aberrant vessel at the hiatus fallopii. Transfusion in these cases was rarely necessary. In 1 case the carotid artery was opened through a dehiscence in the bone of the middle fossa. The patient recovered with transfusion.

The temporal lobe was lacerated by pressure of the retractor in 1 instance, and in another case it became necrotic due to cortical thromboses.

Tumor was encountered in 4 cases. In 1 there were carcinomatous nodules just posterior to the foramen rotundum, and in 1 a meningioma was found on the petrous ridge dipping into both posterior and middle fossae. It was necessary to close the incision in the temporal region and resort to a suboccipital approach. In the third case a carcinoma of the nasopharynx was found which had infiltrated upward and posteriorly into the Gasserian

ganglion. The fourth tumor observed was dark blue and pulsating, and was regarded as a true aneurysm.

There were a number of interesting anomalies which were somewhat disconcerting to the surgeons because of the alteration of customary landmarks in the middle fossa. In 2 patients the facial nerve was visualized. In 1 it lay free just anterior to the petrous ridge, and upon stimulation there were contractions of the orbicularis oris and oculi. In the other the facial nerve was seen to protrude from the dura medially and proceed forward and outward through the foramen spinosum. Fortunately, in both cases the nerve was preserved. In 1 case the 6th nerve was identified in an aberrant position and fortunately was spared.

Occasionally the bony structure at the base of the skull was abnormal. One patient had a large opening from the middle fossa into the middle ear. In another there was an anomaly of the petrous ridge with an atypical venous sinus replacing the middle meningeal artery. In 1 case a bony ridge separated the fibers of the 2nd division into two bundles and in another a bony spicule was noted extending forward from the petrous ridge splitting the motor root.

There was bony dehiscence at the base of the skull with exposure of the carotid artery in 3 cases, and in 1 of them the artery was opened.

Postoperative Problems. In 86 per cent of the 411 uncomplicated cases the patients were discharged within 1 week, most of them going home on the 6th postoperative day. Two of these patients left the hospital as early as the 2nd day.

There were significant postoperative problems in 142 cases. These ranged from continued pain requiring reoperation, abnormally severe herpes, minimal or major eye problems, and facial nerve palsies to cerebrovascular accidents and death.

Only 3 of the 553 patients had to be reoperated upon immediately after the initial procedure in order to accomplish a more extensive sectioning of the root fibers because the original differential section had not been sufficiently complete.

A moderate to severe degree of keratitis was observed in 84 patients (15.1 per cent of those operated upon), but in 41 this presented no problem in treatment. Forty-three of the keratitis patients (7.9 per cent of those operated upon) required a tarsorrhaphy. Of the 84 patients with keratitis the 1st division of the 5th nerve had been sectioned or damaged in all but 8. Therefore in only 9.5 per cent of the individuals with keratitis had the 1st division been preserved. Six patients of this latter group required tarsorrhaphy. These figures indicate the importance of preserving the 1st division whenever possible in order to prevent this unfortunate complication. There was one tragic case in which the keratitis was neglected, and the patient subsequently came to enucleation of the eye.

Inadequate records were kept on the postoperative testing of the motor root so that a fair evaluation of this problem is not possible. However,

we have been fortunate enough to have had no cases of bilateral impairment of the motor root function postoperatively in patients who have had rhizotomies for bilateral tic pain.*

In 16 patients, 2.8 per cent, there was an immediate complete facial palsy. In 21 cases, 3.7 per cent, a delayed facial palsy occurred; 18 of the latter appeared within the first 4 days postoperatively while the other 3 occurred as late as 10, 11, and 14 days after operation.

Two patients had a complete 6th nerve palsy postoperatively.

Minor postoperative problems may be recorded. Ten patients were transiently disoriented and another patient continued to suffer from an organic brain syndrome. In 4 cases there were wound infections and in 2 others there was moderate wound separation. Cardiac failure occurred in 2, pulmonary tuberculosis flared up in 1, parotid abscess was present in 1, hysteria in 1 and urinary infection was a problem in 4.

Deaths. The operative mortality rate was 1.6 per cent, with 9 deaths, which we do not regard as too high when one considers the age group involved, the numerous preoperative complications and the number of surgeons. One hypertensive patient, 56 years of age, succumbed on the operating table, and another, 84 years old, with marked cerebral arteriosclerosis, died 45 days postoperatively. Both had suffered cerebrovascular accidents. The remaining 7 patients died within 3 days of operation. Preoperatively 5 had hypertension (1 had syphilis in addition), and their blood pressures fell precipitously during the procedure with subsequent cerebral thrombosis. Another of these 7, aged 77, suffered a laceration of the temporal lobe, followed by intraventricular hemorrhage and death. The most tragic death was that of a 36-year-old woman in whom a softening of the temporal lobe developed, probably from too marked retraction of the lobe by the assistant during the operative procedure. She died 3 days postoperatively. With the exception of this patient the others who had succumbed were over 50 years of age and had been troubled with cardiac, cerebral, or luetic disease preoperatively. It is believed that at present we are decreasing our mortality rate by using intravenous sodium pentothal as an adjunct to local anesthesia, thereby abolishing the shocking pain stimulus which tends to cause hypotension. The application of bladder tourniquets to the extremities or an antigravity suit might also prevent sudden drops in pressure since all of these patients were operated upon in the upright position. This would be more satisfactory than the use of vasoconstrictors where there is danger of a hyperresponse to the medication. The latter group of drugs should be reserved for acute precipitous hypotensive episodes.

Follow-up on Rhizotomies.

Since many of our patients were elderly and lived at great distances, the follow-up study had to be carried out by means of questionnaire. This

* Dr. Peet's closest associates do not recall ever seeing him divide a motor root where the ganglion was not infiltrated by tumor.—R.C.S.

attack upon the problem is not an ideal one, but by careful selection of questions, we believe that we learned a number of interesting things.

Of the 689 patients who had been examined in this 10-year-period for their trigeminal neuralgia, replies were received concerning 447, or 65 per cent. Of the 553 patients who had had trigeminal rhizotomies, 338 answered their questionnaires and another 44 had died but were reported upon by their relatives, a response of 69 per cent.

Time Elapsed since Operation. Of the 553 patients, 160 reported within the first 4 years after operation; there were 25 additional patients who had succumbed, but about whom we had information postoperatively. Replies were received from 145 individuals who had been operated upon 5 to 10 years before; 13 others in the group died, but were reported upon. Thirty-two were in their 11th postoperative year; 7 other patients falling in this category had died but reports had been returned concerning their postoperative condition.

Age. There were 111 patients who were alive and over 60 years of age. Sixty individuals were over 75 years, 6 were over 85 years, and one man was over 90 years of age. Those who were over 85 years old had been operated upon 2, 3, 4, 5, and 7 years prior to the questionnaire. The patient over 90 years of age reported 5 years postoperatively. These figures tend to indicate that relief of symptoms by operations is justified and worthwhile even in the late seventies or eighties.

Relief of Pain. Complete relief of *all* types of discomfort, including the unpleasantness of any type of paresthesia, was accomplished in 111, or 29 per cent of the 382 patients who had had rhizotomy and replied to the questionnaire.

Paresthesias. Crawling and drawing sensations were complained of by 213 patients, or 55.7 per cent of the 382 operated upon. There were 116, or 30.4 per cent, who had burning pain. It is interesting to observe that only 16 individuals, 4.1 per cent, complained of numbness in their face, but this was regarded by them as minimal compared to the tic pains. This figure suggests that the importance of preoperative injection with alcohol to determine whether the patient will complain of numbness postoperatively has been overemphasized, but it does permit the evaluation of possible future paresthesias.

Recurrence of Pain. Fifty-four of the 382 patients who replied stated that they had had recurrence of their tic pain. Since differential section was frequently performed, in 33 of these instances the discomfort appeared to be in the distribution of the fibers that were regarded as intact at operation, and pain probably occurred in these residual fibers.

It would appear that in 21 instances, or in 5.4 per cent of the cases, there was recurrence of the pain from which the patient had suffered preoperatively. There are probably several reasons why this figure is so high. Since the questionnaire there has been an opportunity to re-evaluate a few of these people very carefully, and it has been discovered that they had

misinterpreted paresthesias as tic pains. In a few instances there may have been erroneous diagnoses of trigeminal neuralgia which should have been called atypical facial pain.

Facial Palsy. In 37 patients, 6.5 per cent, some degree of facial palsy developed. In 16 of these patients the palsy was immediate and complete, but in the remaining 21 the paralysis was delayed, and 6 of the latter group showed only a paresis.

Upon follow-up, 8, or 50 per cent, of the patients with immediate complete facial palsy had fully recovered and 1 had improved markedly. The remaining 7 in this group did not respond to questionnaire, and it was discovered later that 2 had died.

Fourteen patients, 66 per cent, with delayed facial palsies had recovered completely, and 1 had improved. There were 6 others in this category upon whom we are unable to report because 3 had succumbed and 3 others did not answer.

These findings indicate that an immediate complete facial palsy postoperatively does not necessarily imply that the disability will be a permanent one. In no instance were we informed that a complete facial palsy remained, but perhaps the persistence of this complication was the reason that the remaining 8 of the group of 37 had left their questionnaires unanswered.

II. ALCOHOL INJECTIONS

The various aspects of alcohol injection should be considered separately. In general the policy of this clinic was one of recommending operation rather than alcohol injection feeling that the former procedure correctly performed caused no greater discomfort than injection and that permanent rather than temporary relief was advisable. The patients have been divided into two categories: Group A—those who had injections only; and Group B —those who had been injected previously but later were operated upon at the University Hospital.

Group A. (Injection Only)

Forty-nine patients were injected at the time of their initial examination at University Hospital, and were not operated upon. These injections were carried out by 6 neurosurgeons, but 50 per cent of them were performed by one man. A total of 72 injections was made. If the first one gave only transient or no relief, further injections were frequently performed so that some patients had multiple ones.

Complications. Diplopia developed in 1 patient when the ganglion was accidently injected. There were no corneal complications or deaths.

Immediate Results. In 7, 14.2 per cent of the 49 patients, there was complete failure to relieve the pain. The remaining 42 had at least temporary relief.

Follow-Up

Twenty-seven patients, 55 per cent, responded to the questionnaire.

Duration of Relief. Six had relief of pain for less than 1 week; 7 more had recurrence of pain in less than 2 months. Thus including the 7 initial failures, 20, or 74 per cent, of those upon whom we have data, had relief for less than 2 months. However, 6 patients were relieved for 1 or 2 years, 5 for 3 to 5 years, and 1 for over 9 years.

Recurrence of Tic Pain. Actually in 25 of the 27 injected patients who replied to the follow-up letter there was return of sharp tic pain, but in 2 of these cases the discomfort was in the distribution of fibers that had not been previously injected. Therefore, 23 patients, 85 per cent of this group, had recurrence of their tic pain by the time they had answered their questionnaire.

Paresthesias. As a result of alcohol injection alone, 13 individuals, 48 per cent of those who responded, had crawling sensations; 9, 33 per cent, had burning discomfort; and only 1, 3.7 per cent, complained of numbness of the face. This is a small series but is comparable on a percentage basis with rhizotomies.

Group B. (Injection Preoperatively)

Of the 553 patients who had rhizotomies 199, 34.3 per cent, had had a total of 355 injections preoperatively. Forty-five had had 2 injections, and 47 others had been injected 3 or more times.

Neurosurgeons at University Hospital injected 51 of these patients; qualified neurosurgeons in other institutions performed 20 injections; dentists carried out the procedure on 18 individuals, and the remaining 266 injections were made by the patients' physicians.

Follow-up

Complications. Two patients had residual burning pain in the tongue after the first injection, and this persisted after rhizotomy. Another patient (injected elsewhere) had a slough and excoriation of the face with cartilaginous destruction after the procedure, and a third had a transient facial paralysis.

Duration of Relief. All of the patients in Group B had recurrence of their tic pain causing them to resort to rhizotomy. Fifty patients had only very transient relief of pain after the injections. Twenty-one were pain-free from 1 to 4 weeks, 59 for less than 6 months, 17 from 1 to 2 years, and 9 for 3 or more years before recurrence caused them to seek operation. In the remaining 43 cases the duration of relief was not listed.

In 21 cases in which multiple injections had been given, the period of relief tended to be shorter after each successive procedure, but in 9 cases there was a progressively longer period of relief after each injection.

In 3 instances even though the patients had hypesthesia following

injection and total rhizotomy the tic pain persisted. One wonders whether the correct diagnosis had been made in these cases.

Comment on Injection versus Operation. In Groups A and B, a total of 248 patients had 427 injections. Twenty-three of the patients had relief for 1 to 2 years, 14 for 3 or more years, and the longest period of freedom from pain was 9 years for 1 person. Therefore, only 15.2 per cent of the patients who had injections were asymptomatic for a period of over 1 year.

III. UNTREATED PATIENTS

Follow-up

Of the 87 patients who were merely diagnosed as having trigeminal neuralgia, but who were untreated, 36, 41.3 per cent, answered the questionnaire.

Relief of Pain. Four patients had had complete spontaneous remission of their tic pain for 2, 2½, 3 and 6 years, respectively after their initial visit.

Recurrence of Pain. Twenty patients, 55 per cent, had recurrence of their severe tic pain.

Rhizotomy. Three of the patients who had further tic pain were operated upon elsewhere with complete relief of all discomfort, although 1 had a partial residual facial palsy postoperatively.

Alcohol Injection. Nine patients had received alcohol injections elsewhere, and there was complete relief of *all* discomfort in 5 patients for periods of 1 to 3 years. In 3 others there was a 2-week, 6-month, and 8-month interval before recurrence of tic pain. In 1 case the patient suffered from diplopia for 6 months although he subsequently was completely relieved by rhizotomy.

Paresthesias. Burning and crawling paresthesias were troublesome to 5 of the 9 injected patients.

CONCLUSIONS

Trigeminal rhizotomy is a much more satisfactory procedure than alcohol injection in the average case of trigeminal neuralgia, for there has been complete relief of tic pain in all but 5.4 per cent of the patients operated upon. Alcohol injection, on the other hand, in our series relieved only 15.2 per cent of the patients with trigeminal neuralgia for a period of longer than 1 year.

The incidence of complaints of crawling paresthesias (56 per cent), of burning paresthesias (30 per cent), and of numbness (4 per cent) among the postoperative rhizotomy patients is much higher than frequently cited, and probably approximates the percentages of these symptoms after alcohol injection. The great majority of the patients are so overjoyed to have relief of their severe tic pain that they frequently do not voice complaints about these discomforts unless directly questioned about the symptoms.

It is our feeling that the tic douloureux patient is one of the most grateful in the entire field of medicine, provided he has been forewarned about the

unpleasant postoperative symptoms which may be expected in a fairly high percentage of cases.

It should also be reassuring to the referring physician that in only 6.5 per cent of the cases in which operation has been performed has facial palsy occurred, and in no known instance in this series has it been permanent. The operative mortality rate in our entire series has been 1.6 per cent, which is reasonable in a group in which 34 per cent of the patients are over 65 years of age and 10 per cent are over 75, when one considers that the procedures were carried out by 14 surgeons.

SUMMARY

The data on 689 cases of trigeminal neuralgia which were examined over a 10-year period are presented. The series includes 553 patients who had trigeminal rhizotomies, 49 individuals who had received only alcohol injections, and 87 others in whom the diagnosis was made but who remained untreated.

The data include: age, sex incidence, side of involvement, duration of symptoms, division involved, trigger zones, preoperative complications, operations, immediate complications, postoperative problems, and deaths.

Follow-up was accomplished by questionnaire with a 69 per cent response from the patients who had had trigeminal rhizotomy, a 55 per cent return from those who had had alcohol injections only, and a 41 per cent response from the patients who had been untreated, the diagnosis merely having been established. The replies included information on: the relief or recurrence of tic pain, crawling and burning paresthesias, numbness, the status of any postoperative complications, and any further therapy.

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EFFECTS OF INTRACAROTID ADMINISTRATION OF NITROGEN MUSTARD

ON NORMAL BRAIN AND BRAIN TUMORS

J. D. FRENCH, M.D., P. M. WEST, M.D., F. K. VON AMERONGEN, M.D. AND H. W. MAGOUN, PH.D.

Veterans Administration Hospital, Long Beach, California, and the Departments of Surgery, of Anatomy, and of Biophysics, University of California, Los Angeles, School of Medicine

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THE relative effectiveness of intravenous nitrogen mustard in the palliative treatment of neoplastic diseases has been extensively reported since the first clinical trials by Gilman and associates in 1942.[5] Such therapy was found to be of limited value, however, since experience showed that temporary regression occurred primarily in the malignant lymphomas and only occasionally in bronchogenic carcinoma.[6,10,11] The great majority of neoplasms appeared to be resistant to the drug. Recently this concept has been altered by Bierman *et al.*[1,2,3,4] and Klopp *et al.*[9] who devised techniques for the administration of nitrogen mustard in high dosage directly to the tumor by way of its arterial blood supply and found even radio-resistant neoplasms to be responsive under these conditions. This approach is particularly applicable for chemotherapy of primary and secondary tumors of the liver, where the normal parenchyma has a double blood supply and the neoplasm only one,[1] thus permitting selective concentration of the drug in the lesion.

While similar vascular anatomy is not found in the brain, the possibility of treating intracranial malignancies was suggested by reports of such regional therapy, since it was felt that the high resistance of nervous tissue to irradiation might permit administration of a radiomimetic drug in sufficient dosage to damage the neoplasm without destroying normal brain. For this reason, experiments were performed in cats and monkeys to study the effect produced by the injection of HN_2 (methyl bis β—chloroethyl amine) into the carotid artery on function and structure of the brain. These effects were correlated with those observed after similar injections in 3 patients suffering from primary or metastatic cerebral disease.

METHOD AND PROCEDURE

Chronic experiments were performed on 9 cats and 2 monkeys. These animals were anaesthetized with barbiturates and 0.25 to 1.2 mg./kg. body weight of HN_2 was injected into the carotid artery after its exposure in the neck. Postoperatively, frequent observations were made and periodic EEG tracings were recorded by scalp electrodes during the survival period of the animal. At the conclusion of each experiment autopsy was carried out and pathological sections were made of the brain.

Acute experiments were made on 5 cats and 1 monkey in which from 1 to 4 mg./kg. body weight of HN_2 were injected into the internal or common carotid

artery after exposure of the vessel in the neck. In 2 cats, the procedure was carried out under barbiturate anaesthesia. The remaining animals were prepared under ether and immobilized either with Syncurine or by section of the cervical spinal cord, the animal being sustained on artificial respiration. Electrocortical activity was recorded on a Grass Amplifier and Inkwriter before, during, and after injection from screw electrodes in the calvarium. In one animal, HN_2 was applied to the cortex directly on a piece of filter paper, and later a small amount was injected directly into the brain.

Clinical observations were made following the injection of 0.20 to 0.27 mg./kg. of body weight of HN_2 into the exposed internal carotid artery in 3 patients suffering from neoplastic disease involving the brain. The drug was dissolved in saline, 0.5 mg./cc., and given at the rate of 1.0 mg./min. One patient received an equivalent additional injection 6 weeks after the first because of recurrence of symptoms. The brains were studied at autopsy in all instances.

TABLE 1

INTRACAROTID HN_2 - CHRONIC ANIMAL EXPERIMENTS

SINGLE INJECTION

DOSAGE	ANIMAL #	BRAIN DISTURBANCE	FACE DISTURBANCE	SURVIVAL PERIOD (DAYS)
1 MG/K OR OVER	CAT 4	+		2 DAYS
	CAT 16	+	+	4 DAYS
	CAT 17	+	+	7 DAYS
.75 - .90 MG/K	CAT 1	+	+	16 DAYS
	CAT 6	+	−	4 DAYS
	CAT 14	+	−	23 DAYS
.50 MG/K	CAT 8			10 DAYS
	CAT 12	+	+	7 DAYS
	MONKEY 2	+	+	42 DAYS (SACRIFICED)
.25 MG/K	MONKEY 1	+	−	42 DAYS (SACRIFICED)

TWO INJECTIONS 7 DAYS APART

DOSAGE EACH INJECTION				
.75 MG/K	CAT 13	+	+	10 DAYS
.50 MG/K	CAT 9	+	+	30 DAYS (SACRIFICED)
.25 MG/K	CAT 11	−	+	30 DAYS (SACRIFICED)

RESULTS

ANIMAL OBSERVATIONS

The results of the chronic experiments are summarized in Table 1. All but 1 animal (Cat 11) manifested some degree of brain disturbance following the injection, varying from transient EEG changes (Monkeys 1 and 2, Cat 9) to marked hemiparesis, cerebral edema, and death. When

neurological symptoms occurred, they were usually present the day following injection, but were occasionally delayed for as long as 6 days, even with large doses (Cat 17). In fact, Cat 1 appeared to be perfectly normal, after a slight ataxia and hemiparesis the first post-injection day, until it became comatose and expired 14 days later. Only 2 of 11 animals who received

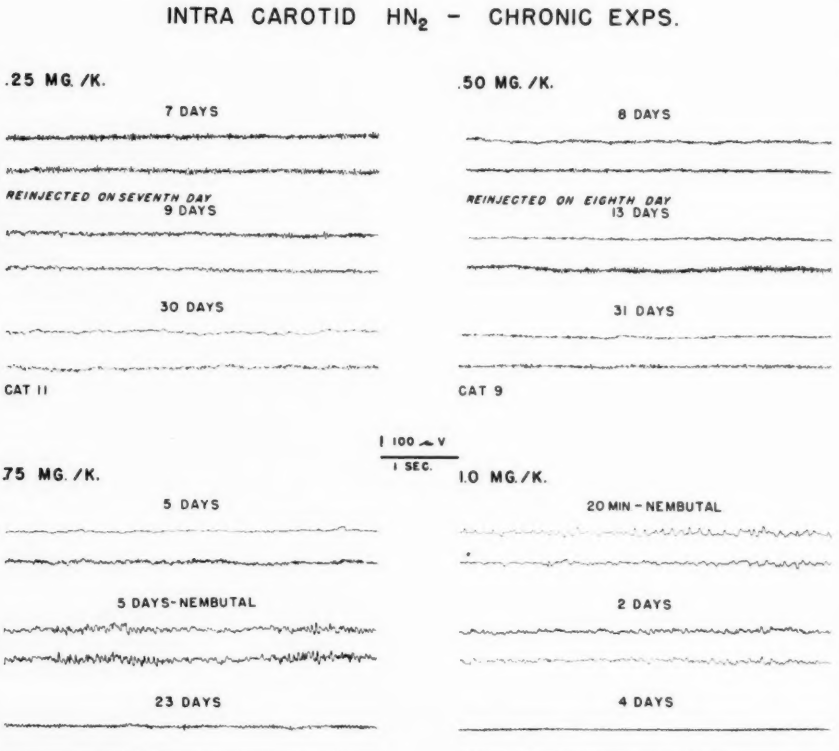

FIG. 1. EEG changes in cats during the chronic period following intracarotid injection of 0.25, 0.50, 0.75, and 1.00 mg./kg. of nitrogen mustard (upper channel in each strip injected side). Length of time after injection is indicated above each record. Note reduction of amplitude of electrical activity in each case; also slow waves in Cat 16 after short latent period, as in acute experiments.

regional doses of 0.50 mg./kg. body weight or more survived, and all 7 animals who received 0.75 mg./kg. of body weight or over succumbed. The 2 animals who received 0.25 mg./kg. of body weight survived. Some degree of soft-tissue disturbance of the face, varying from swelling or discharge in the eye, nose, or mouth to severe necrosis of the tongue, was observed in 8 of the 13 animals.

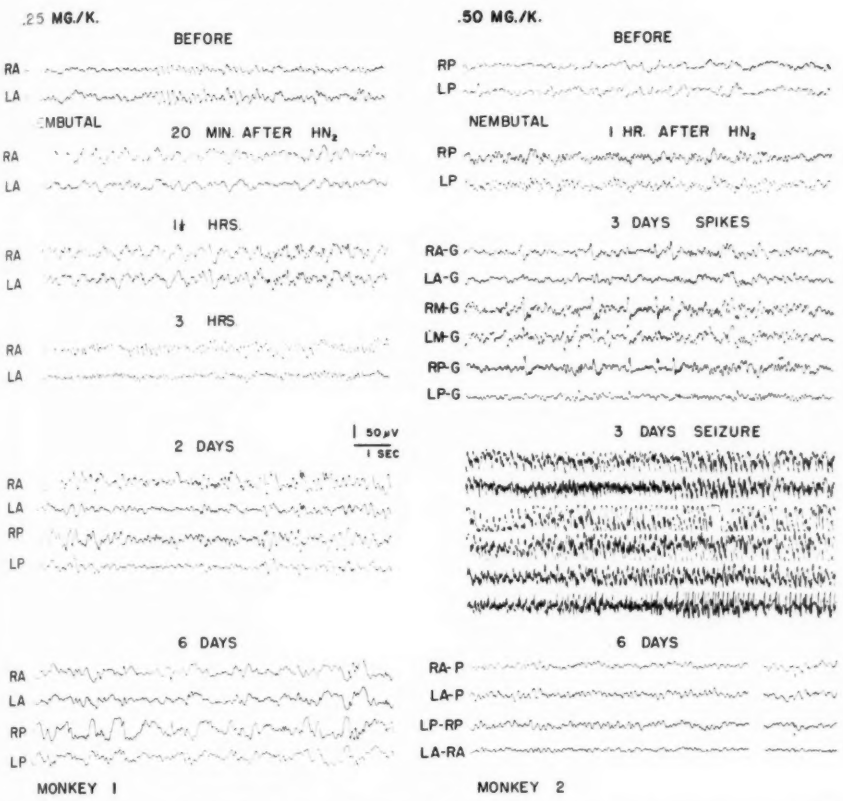

FIG. 2. EEG changes following intracarotid injection of 0.25 and 0.50 mg./kg. of body weight of HN_2 into right internal carotid artery of monkeys. Note large slow waves developing in Monkey 1 after short latent period with later appearance of spikes on the injected side. In Monkey 2, spikes predominate on the injected side and seizure activity is shown on the 3rd day. A=anterior, G=ground, L=left, M=middle, P=posterior, R=right.

The effect of these injections on electrocortical activity in the chronic animals is summarized in Figs. 1 and 2. There was usually a latent period, varying from 2 to 10 days, between the time of injection and the development of abnormality, during which the tracing appeared to be perfectly normal. Characteristically, the tracing showed asymmetry in cats, the injected side having a much lower amplitude, with some slight slowing of rate, than the uninjected side. A transient acute effect was also noted 20 minutes after the injection in the anaesthetized survival animals (Cat 16, Fig. 1; Monkey 1, Fig. 2) manifested by the development of high-voltage

slow activity on the injected side. The chronic voltage suppression persisted throughout the duration of the experiment in cats.

The appearance of the post-injection EEG in surviving monkeys was somewhat different from that observed in cats. Here, the same transient slow-wave activity was seen some 20 minutes after injection, but the effect was more sustained (Fig. 2), persisting in Monkey 1 for many days. In

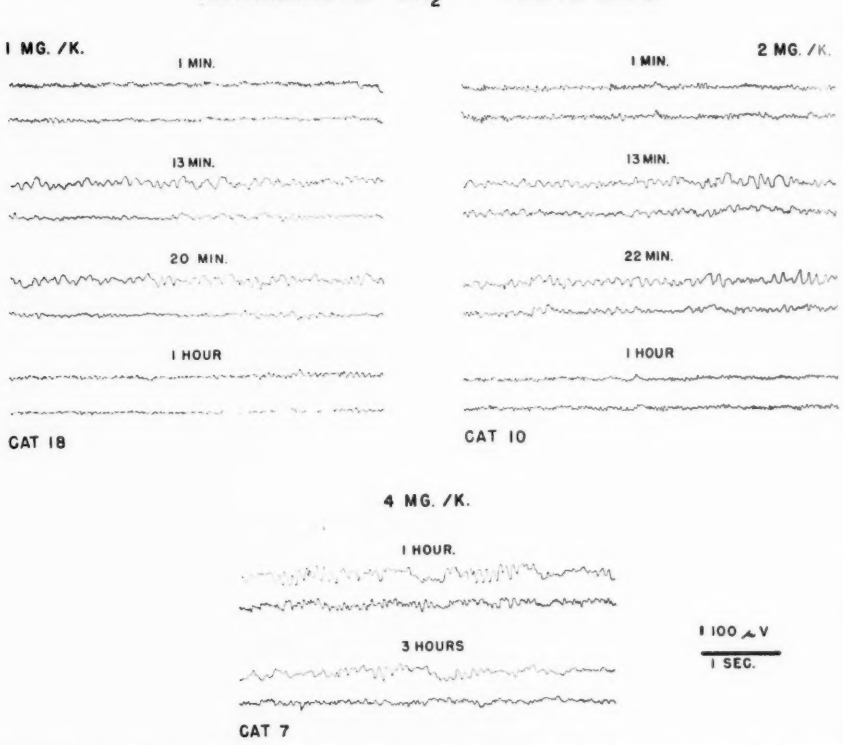

FIG. 3. EEG changes following intracarotid injection of 1.0, 2.0, and 4.0 mg./kg. of body weight of HN_2 in cats. Cats 18 and 10 were immobilized with Syncurine, and Cat 7 was an *encephale isolé*. Note appearance of large slow waves on injected side (upper channel in each strip) after a latent period, with subsequent disappearance in animals with smaller doses.

Monkey 2 (0.50 mg./kg.), spike activity was prevalent diffusely, but much more intense on the injected side, and grand mal seizures were frequent for 4 days (Fig. 2). Even 6 weeks after injection the tracing on both chronic animals was abnormal.

In all acute experiments larger doses of HN_2 were used in order to intensify the effect for better study (Figs. 3 and 4). In cats, no change in the EEG was apparent until 13 to 15 minutes had elapsed, at which time slow

wave activity was observed on the injected side. This effect persisted for approximately an hour, following which it disappeared in animals who received 1 to 2 mg./kg. body weight. When 4 mg./kg. body weight was employed, however, the changes remained for a full 3 hours. When HN_2 was applied directly on or injected into the cortex, no alteration in the EEG was noted.

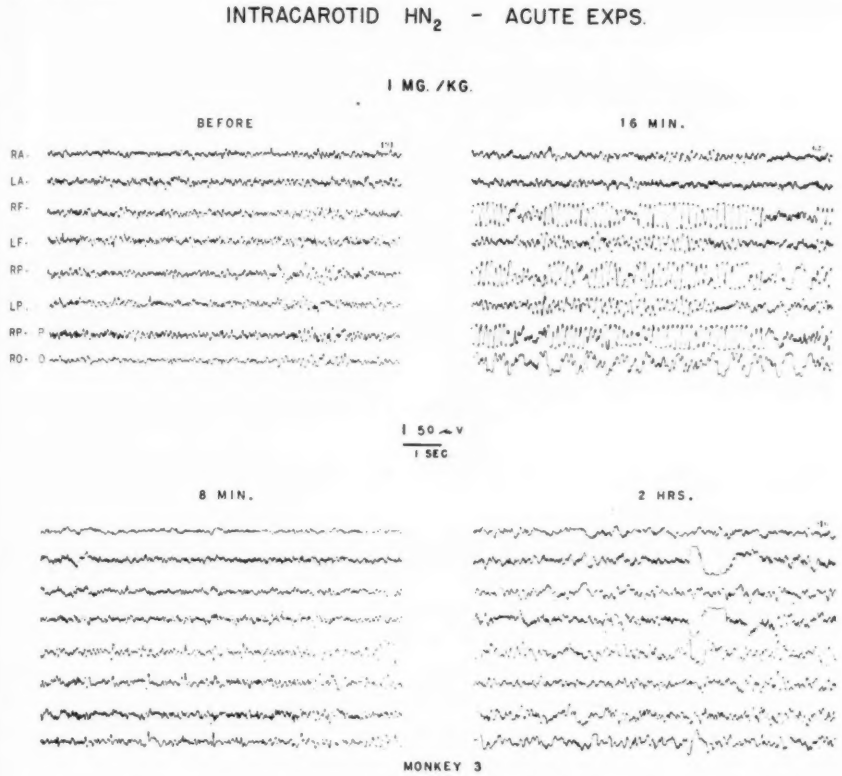

FIG. 4. EEG changes following injection of 1 mg./kg. of body weight of HN_2 into right carotid artery of a monkey. Note spike activity in right RP-O at 8 minutes. Large slow waves first appeared at 16 minutes on injected side as in cats. Effect had largely disappeared in 2 hours. A=anterior, F=frontal, L=left, O=occipital, P=parietal, R=right.

In the monkey injected with 1 mg./kg. body weight, spike activity occurred on the injected side after 8 minutes, to be replaced 8 minutes later by large slow waves (Fig. 4). This abnormality had largely disappeared in 2 hours.

The EEGs in these acute and chronic experiments indicated, therefore, that an initial change occurred in the tracing some 8 to 16 minutes after injection of as little as 0.25 mg./kg. HN_2 (Monkey 1, Fig. 2) and disap-

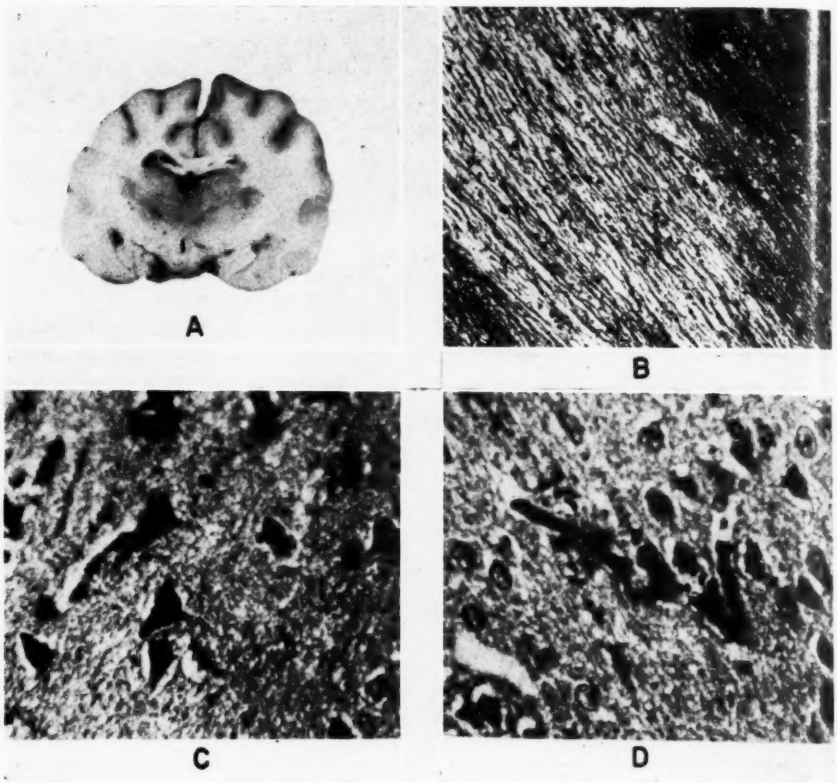

FIG. 5. Cat 4. (A) Photograph of sectioned brain 2 days after injection of 1.0 mg./kg. into right carotid artery. Note edema on injected side. (B) Photomicrograph of the edematous white matter (hematoxylin and eosin). (C) Severe acute toxic change of the neurones. (D) Capillary congestion with diapedesis of red blood cells.

peared 1 to 2 hours later, even after much larger doses had been employed. Days later, depending on the dose injected, asymmetry of the tracing developed, the injected side showing low-voltage activity, as compared to the uninjected.

Pathologically, a variety of effects were noted depending upon the amount of HN_2 injected. The brains of acute animals, sacrificed 2 or 3 hours after the injection of HN_2, showed no gross abnormality. Microscopically, however, areas of relative ischemia, in which the arterioles were markedly constricted, alternating with areas of congestion, were found to be present.

The chronic animals who succumbed within 2 or 3 days after operation showed marked edema on the injected side (Fig. 5). Microscopically, in addition to the edema, petechial and ring hemorrhages were prevalent and

congestion was severe. Acute cell change of the neurones was present in patchy areas, alternating with regions in which the cells had a relatively normal appearance.

The brains of animals surviving longer, hence, in most instances, those who received smaller injections, showed no abnormality grossly. Microscopically, however, there were demonstrated varicose degenerated vessels, some containing thrombi, with large numbers of perivascular phagocytes, chronic neuronal degeneration, areas of demyelinization, and increase in cortical glia. All changes were distinctly worse on the injected side, but were present to some degree diffusely in a patchy manner. Least affected were the cats and monkeys who survived longer than 3 weeks, when relatively little abnormality was seen.

CLINICAL OBSERVATIONS

The results of 4 injections of HN_2 into the carotid artery in 3 patients are summarized in Table 2. The improvement in patient A.B. with metastasis

TABLE 2

INTRACAROTID HN_2 – CLINICAL CASES

NAME	DIAGNOSIS	AMOUNT HN_2 INJECTED	RESPONSE	LIVED AFTER HN_2
A.B. 1ST INJECTION	BRONCHOGENIC CA: CEREBRAL METASTASIS WITH RT. HEMIPLEGIA	.20MG/K	MARKED IMPROVEMENT HEMIPLEGIA CLEARED	7 WEEKS
A.B. 2ND INJECTION	RECURRENT HEMIPLEGIA 6 WEEKS AFTER 1ST INJECTION	.25MG/K	POOR	4 DAYS
G.H.	OLIGODENDROGLIOMA RT. HEMISPHERE: MALIGNANT	.27MG/K	SLIGHT TEMPORARY IMPROVEMENT	5 MONTHS
E.H.	BRONCHOGENIC CA: CEREBRAL METASTASIS	.23MG/K	POOR	15 HOURS

from bronchogenic carcinoma was highly gratifying after the first injection. This improvement, however, lasted only 5 weeks, and a second injection resulted in a fatality. Little transient improvement resulted in patient G.H. who had a primary brain tumor (malignant oligodendroglioma). Patient E.H., with multiple metastases in the brain from a bronchogenic carcinoma, died of acute cerebral edema 15 hours after injection, never having regained complete consciousness.

Pathologically, the brain of A.B. (who succumbed 4 days after a second injection) showed severe edema, not only on the side of injection, but in a circumscribed area contralaterally (Fig. 5). Microscopic sections of the small metastatic nodule in the left hemisphere showed considerable necrosis of the metastasis, which was not seen in a similar nodule in the cerebellum approximately two-thirds as large. The area surrounding the affected

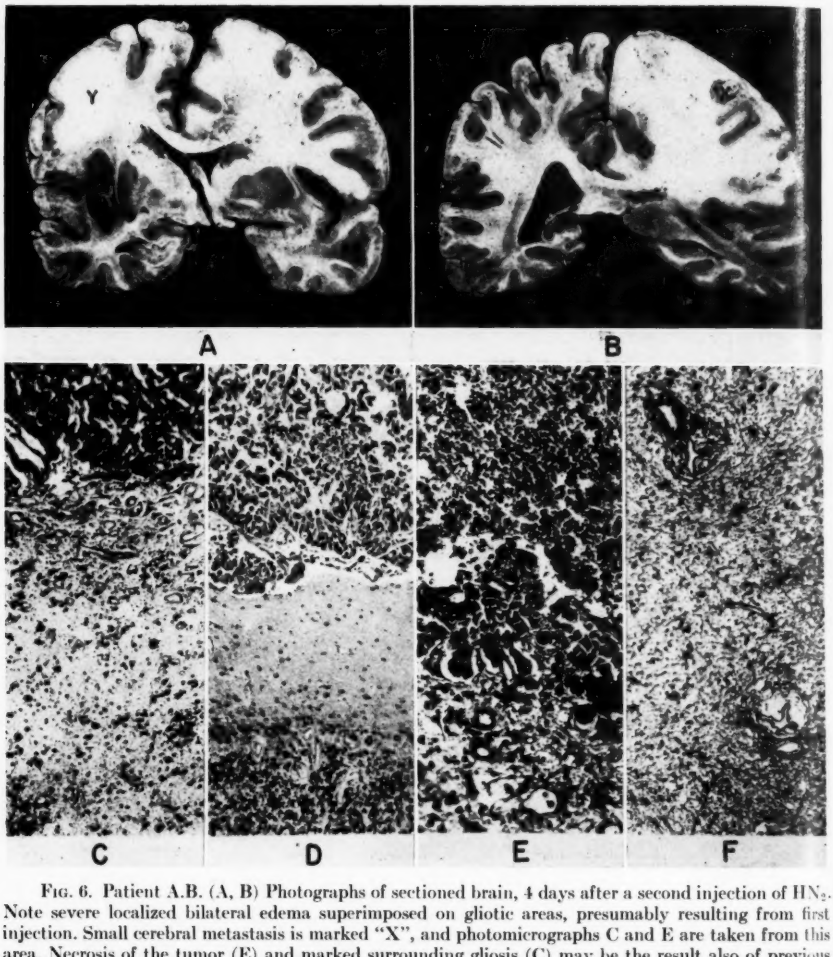

FIG. 6. Patient A.B. (A, B) Photographs of sectioned brain, 4 days after a second injection of HN_2. Note severe localized bilateral edema superimposed on gliotic areas, presumably resulting from first injection. Small cerebral metastasis is marked "X", and photomicrographs C and E are taken from this area. Necrosis of the tumor (E) and marked surrounding gliosis (C) may be the result also of previous injection, while petechial hemorrhages (C) are probably associated with recent injection. Sharp outlines and absence of necrosis or gliosis in cerebellar nodule (D) are in marked contrast with this. (F) is a photomicrograph of area marked "Y" on contralateral side showing the same changes as the area around the cerebral metastasis, indicating contralateral spread of injected HN_2.

nodule—in fact, the larger part of the entire left hemisphere—showed extensive demyelinization and gliosis, undoubtedly resulting from the earlier injection of HN_2 7 weeks before, as well as petechial hemorrhages and edema from the more recent one. Such changes were not seen in the area surrounding the cerebellar nodule which, since it was not vascularized by the carotid, had not been exposed to HN_2. The area labeled "Y" on the contralateral hemisphere showed changes exactly similar to those seen on

the injected side, indicating spread of the HN_2 to this area. It appeared, therefore, that the return of symptoms in this case was the result of progressive toxic degeneration from the injection rather than from enlargement of the metastatic nodule.

Patient G.H. had such extensive cerebral changes in the brain resulting from a long history of cerebral oligodendroglioma complicated by 3 operations that the results of HN_2 injection 5 months prior to death could not be assessed. Patient E.H., however, who succumbed 15 hours after the injection of HN_2 for multiple cerebral metastases, showed microscopically diffuse edema and multiple petechial hemorrhages primarily on the side of injection.

In summary, the animal experiments have shown that both an acute and a chronic effect follow the injection of HN_2 into the cerebral circulation. The acute effect occurs after a latent period of minutes, manifest by the appearance of slow waves in the area bathed by injected vasculature, and appears to coincide with the period of vasomotor change noted in sacrificed acute preparations. Some alteration in the EEG could be obtained by unilateral occlusion of the carotid artery in the neck, but was never as clear-cut or distinct as that following injection of HN_2. It appears, therefore, that a relative anoxemia is produced by effect of the substance on the peripheral vascular tree. This mechanism is further suggested by the fact that HN_2 injected directly into the cortex did not cause alteration in the EEG. The chronic effect occurred days to weeks later, being manifested by the onset of neurological and soft tissue changes, as well as by amplitude asymmetry of the EEG with the voltage being lower on the injected side. This period appeared to be correlated pathologically with toxic changes in the neurons and with glial proliferation, or, in cases where larger amounts were used, with edema, petechial hemorrhages and acute neuronal change.

These manifestations were also observed to some degree in the clinical cases. The pathological alterations in patients E.H. and A.B., showing edema and petechial hemorrhages soon after injection, were similar to the changes observed in the animal brains where death occurred after a similar interval. The microscopic sections in patient A.B. also showed late chronic effects characterized by destruction of parenchymatous tissue, and its replacement by extensive gliosis in areas bathed by the injected HN_2. While it is true, therefore, that tumor necrosis occurred after injection, it is equally certain that severe parenchymatous destruction resulted from use of the material.

DISCUSSION

The surprising sensitivity of normal brain to relatively small doses of intra-arterial nitrogen mustard appears to contradict the generally accepted views that nervous tissue is highly radio-resistant and that the mustard compounds have radiomimetic actions. Although the mustards are known to inhibit mitosis and cause nuclear fragmentation[5] it is at once apparent from these studies that the drug has other more rapid and toxic effects

which make the comparison with irradiation inappropriate. Chief among these is the almost immediate damaging effect on normal cerebral arterioles, resulting in spasm, altered permeability and extravasation of cells and fluid. This may be due to the ability of nitrogen mustard to combine promptly with cellular nucleoprotein[7] thus destroying the function of the endothelial membrane. An additional fact which may contribute to the intolerance of the brain for this agent is that certain enzymes, the phosphatases, choline oxidase and acetylcholine esterase, all of which are particularly high in nervous tissue, are among the few enzyme systems that exhibit a high degree of sensitivity to mustard compounds.[5]

The use of often-repeated tiny doses of HN_2 injected into the carotid artery as described by Klopp *et al.*[8] was not investigated here. Their animals, however, subjected to presumably similar total doses as some of ours, showed severe brain changes and the follow-up period of 2 patients so treated was not inconsistent with that in 2 of the clinical cases reported here.

Limiting factors in the intracarotid use of HN_2, no matter what the dose or frequency of injection, would seem to be not only the obvious toxicity of the substance to normal brain tissue but the apparent impossibility of controlling its dispersion into the diseased area alone. In animals and patients alike toxic effects were either diffuse, involving frequently both hemispheres, or patchy, indicating that any part of the intracranial vascular distribution could receive the bulk of the injected substance when instilled in an area as remotely situated as the main trunk of the vessel in the neck. Selective absorption of HN_2 into an area containing a neoplasm by virtue of a local alteration in the blood-brain barrier appears impossible due to the marked endothelial toxicity of the substance.

Regardless of the basic causes for the intolerance of the brain to nitrogen mustard, the existence of the fact makes this chemotherapeutic approach to cerebral neoplasms extremely hazardous. Even though one may be fortunate enough to achieve encouraging palliation with disappearance of neurological symptoms in a patient after the first injection, the probability that undetectable vascular and parenchymal damage has been produced should be borne in mind since repetition of the treatment under such circumstances may precipitate an acute fatal reaction. Because there is little or no margin of safety when nitrogen mustard is given by way of the internal carotid artery in the manner described herein, the authors feel that in spite of the urgency of the clinical situation, this form of chemotherapy is generally contraindicated.

SUMMARY

1. Acute and chronic experiments were carried out on animals involving the intracarotid injection of nitrogen mustard to assess the feasibility of employing this procedure in the treatment of intracranial neoplasms.

2. Observations were reported on 3 patients with brain tumors in whom such injections were made.

3. It was concluded that HN_2 is too toxic to normal endothelium and brain tissue to make its use in this capacity possible.

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AN EVALUATION OF PALLIATIVE SURGICAL PROCEDURES IN TRIGEMINAL NEURALGIA

EVERETT G. GRANTHAM, M.D., AND LUDWIG H. SEGERBERG, M.D.
Department of Surgery, University of Louisville, School of Medicine, Louisville, Kentucky

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IT IS generally understood that sensory root section by the temporal route is the operative procedure to give lasting relief from the pain of trigeminal neuralgia. Some writers, however, agree that there are indications for less radical or palliative procedures which must be considered in many instances. It is our purpose in this paper to give further consideration to the palliative procedures that are commonly employed: alcohol injection of branches of the trigeminal nerve; or avulsion of peripheral branches of the trigeminal nerve.

It is felt that standard text and reference books are negligent in not giving more discussion of the usefulness of palliative operative procedures, especially avulsions, for the relief of major trigeminal neuralgia. Some textbooks[5] make no mention of the palliative procedures; others[1,2,4,8,14,15] refer briefly to the use of a palliative procedure but discuss only alcohol injection. The popularity of alcohol injection is shown in the statement of Dandy:[3] "Injections of alcohol have now almost superseded neurectomies. By either method the relief is only temporary, rarely being longer than 18 months and usually much less." In the same reference work Peet[10] stated: "Avulsion or section of the peripheral nerves is never indicated, with the possible exception of the supra-orbital, since alcohol injection gives relief of equal duration and leaves no disfiguring scar." Grant[7] stated that he does not believe in avulsion of any of the peripheral branches of the 5th nerve other than the supra-orbital, since, in his opinion, injection of the 2nd and 3rd divisions produces a greater area of anesthesia. He does point out, however, that 4 or 5 years of relief may be obtained by supra-orbital avulsion.

Perhaps the foremost indication for a palliative procedure is an aged patient in a debilitated state in whom a craniotomy would be hazardous. A second indication for a palliative procedure is neuralgia confined to the 1st division of the trigeminal nerve, or pain from involvement of only the 1st and 2nd divisions of the trigeminal nerve. One hesitates particularly to produce a corneal anesthesia in the original operative procedure. It is not uncommon to hear the complaint of a patient that had he known what he was to experience in the way of facial anesthesia he would not have submitted to the surgery. This complaint is less apt to occur if a palliative procedure is first employed and followed by the permanent procedure when the pain recurs. Perhaps even more disturbing to the patient are the dysesthesias that occasionally occur. We have had patients with typical major trigeminal neuralgia due to multiple sclerosis. In such patients, a palliative

procedure, rather than a permanent division of the fibers of the 5th nerve, is indicated. Occasionally it is difficult or impossible to be certain whether a patient has one of the atypical facial neuralgias or tic douloureux. In such cases a palliative procedure may be indicated for obtaining a differential diagnosis and to prevent a permanent error. Finally, it is our experience that if patients are presented with the possibilities of the temporary and the permanent type of procedure and then given the opportunity to make their choice between the two, many will elect the palliative procedure for the original operation.

We disagree with Peet and Echols[11] who stated, "A poor excuse for performing this procedure [temporary interruption of 5th nerve function] is that it will teach how anesthesia of the face feels. It is highly improbable that any patient suffering from severe trigeminal neuralgia ever refuses the intracranial operation because he did not like the anesthesia which a nerve injection temporarily produced." This is probably true, but it does not alter the fact that if the patient has the permanent operation originally, he may be unhappy about it. We, therefore, agree with Sachs[12] who stated, "Following the radical operation, there is a permanent anesthesia which some patients find extremely annoying; following an alcohol injection there is the same type of anesthesia but it is transient, and when the nerve regenerates the anesthesia disappears. If the patient knows what the anesthesia following an alcohol injection feels like he subsequently accepts more willingly the permanent anesthesia which follows operation."

There seems no doubt that alcohol injection of the branches of the 5th nerve is the most widely used of palliative procedures in spite of the fact that it is a most trying ordeal for both the patient and the surgeon—one that many surgeons are anxious to avoid if possible. Many patients are unwilling to submit to a second injection because of the intense pain experienced in the correct placement of the needle at the original procedure. Another disadvantage of alcohol injection is that it is unsuccessful in a fairly high percentage of cases. Grant[6] reported a successful block in approximately 80 per cent of the cases in his series. In addition, there is an occasional occurrence of an extra-ocular palsy or of a facial paralysis. We have seen a patient injected at another clinic in whom total blindness resulted from infiltration of the alcohol about the optic nerve. Sweet[13] advocated the use of radiographic control for the placement of the needles for an alcohol block of the branches of the 2nd and 3rd divisions, and this undoubtedly is an advantage in obtaining a correct placement of needles and a higher percentage of effective blocks.

The relief of pain from a successful alcohol block generally lasts no longer than 6 to 18 months. The duration of relief in Grant's[6] cases averaged 11 months for the 1st division, 14 months for the 2nd division and 16 months for the 3rd division. Horrax and Poppen[9] had an average relief of 6 months for the supra-orbital, 12.4 months for the infra-orbital, 12.4 months for the maxillary and 14.3 months for the mandibular. Longer periods of relief

occasionally occur, but these are not the rule, and one cannot with any degree of assurance promise the patients more than 1 year of relief. Sweet[8] reported that with radiographic control the average relief of pain from injection of the 2nd division was 7 months. Of 54 patients in whom 3rd division injections had been made, 30 were followed; they had had relief of pain for an average of 30 months. This is an unusually long period of relief following an alcohol injection and one wonders if it does not result from infiltration of the alcohol into the gasserian ganglion which ordinarily is looked upon as a dangerous procedure to attempt deliberately. In any event, alcohol injection of the 3rd division provides longer relief than that obtained in 2nd division blocks.

Avulsion of the supra-orbital and/or infra-orbital nerves in trigeminal neuralgia of the 1st and/or 2nd divisions is a simple and relatively benign procedure. The avulsion can be accomplished with practically no discomfort to the patient. It is a far less terrifying experience to the patient than an alcohol injection. Hospitalization is required but the patients can return to their homes after 3 days. In fact, most patients can leave the hospital within 24 hours and have the sutures removed in the out-patient department.

Avulsion of the branches of the trigeminal nerve has been mentioned by many writers as an adequate palliative procedure, but has been given very little attention. The use of alcohol injection has occupied the limelight in descriptions of the palliative procedures. It is our feeling that this is an injustice to a most valuable procedure. For this reason we have made an analysis of the private patients treated in one hospital from 1935 to 1949.

A total of 151 patients with trigeminal neuralgia have been treated. It is of interest to note that the right side of the face was involved in 100, the left side in 47, and in 4 patients the lateralization was not recorded. A similar predominance of the right side has been noted by Grant,[6] and Horrax and Poppen.[9] The involvement of the branches of the 5th nerve in our series was as follows:

1st division	2 cases
2nd division	37 cases
3rd division	29 cases
1st and 2nd divisions	39 cases
2nd and 3rd divisions	30 cases
1st, 2nd and 3rd divisions	14 cases

It is important to note that 51.6 per cent of the patients had their pain confined to the 1st or 2nd division or both the 1st and 2nd divisions. In a series of 468 patients reported on by Horrax and Poppen,[9] 30 per cent had their pain confined to these divisions. It is in this group that avulsion is particularly indicated in preference to alcohol injection.

Of the 151 cases of trigeminal neuralgia in the present series, primary retrogasserian neurotomy was performed in 42. The remaining 109 patients

underwent either alcohol injection or avulsion or both, done either in this clinic or elsewhere, and it is with this group that we are concerned.

Sixty-one alcohol injections were done in the group that had palliative procedures. Follow-up information was obtained on 49 patients. The average duration of relief was 15.5 months, the relief ranging from no relief to 9 years. There were no deaths in the group, but in 1 patient injected elsewhere blindness developed following injection. It is of interest to note that there were 3 patients in the group who reported no relief after the development of anesthesia over the desired distribution following injection, and all 3 obtained relief from posterior rhizotomy.

Seventy-four avulsions were performed in the group of 109 patients. Follow-up information was obtained on 55, and the 19 patients we have not been able to follow all had reported relief at the time of their hospital discharge. The average duration of relief reported by the 55 patients was 33.2 months, the duration ranging from 5 months to 8 years. In a few cases, avulsions were repeated but the majority of the patients underwent retrogasserian neurotomy when the pain recurred. There were no deaths and only 1 complication in the group—a mild postoperative infection following an infra-orbital avulsion.

It is not necessary to describe the technique of supra- and infra-orbital avulsion. There are several factors, however, that we feel are worthy of mention. The choice of anesthesia in most instances is local infiltration with 1 per cent procaine and direct infiltration of the nerve when it is exposed. We have used a combination of sodium pentobarbital 0.1 gm., morphine sulfate 0.08 gm., and hyoscine hydrobromide 0.004 gm. 1 hour preoperatively, and find this is most effective in allaying the natural apprehension of the patient. In many instances the patient has a complete amnesia for the procedure as a result of the premedication. In many cases sodium pentothal has been administered as the avulsion was accomplished, and our anesthesiologists have convinced us that this is a perfectly safe procedure. It probably is important to point out that in order to avoid an external scar, infra-orbital avulsions are done by the intra-oral route. The procedure is an *avulsion*, and every effort is made to remove as much of the nerve as possible in order to delay its regrowth. By grasping the proximal end of the cut nerve in two hemostats and exerting firm traction on it a rather long segment of nerve may be removed. Similarly the peripheral end should be avulsed. We have also found it helpful in the infra-orbital avulsion to insert a needle, insulated except for a $\frac{1}{2}$ cm. point at the tip, into the infra-orbital foramen following the avulsion and to apply heat from the electrosurgical apparatus until charring of the soft tissues results.

The entire procedure of supra- and infra-orbital avulsion rarely requires more than 20 minutes. We maintain the patient on prophylactic penicillin for a period of 72 hours to prevent infection in the postoperative period. We have found the long-lasting penicillin quite effective, and this may be

given by the patient's family physician or in the out-patient department if the patient is discharged prior to the completion of the penicillin therapy.

SUMMARY

We believe the palliative procedures for the alleviation of pain in trigeminal neuralgia have an important place in the proper care of these patients. In the literature alcohol injection has received far greater attention than nerve avulsion as a palliative procedure. It is felt that this is an injustice, since avulsion is simpler and gives more effective relief. This is particularly true if the neuralgia involves the 1st, or the 2nd, or both of these divisions of the trigeminal nerve. Alcohol injection should be reserved for those cases in which the pain is confined to the 3rd division.

An analysis of 109 cases in which palliative procedures were done shows that the average relief from supra- and infra-orbital avulsion was 33.2 months, whereas that from alcohol injection was 15.5 months.

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CASE REPORTS AND TECHNICAL NOTES

AN UNUSUAL CASE OF UNILATERAL EIGHTH NERVE TUMOR

VERNON H. MARK, M.D., AND WILLIAM H. SWEET, M.D.
Massachusetts General Hospital, and Neurosurgical Service, Boston Floating Hospital, Boston, Massachusetts

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The occurrence of bilateral acoustic tumors, or acoustic tumors associated with von Recklinghausen's neurofibromatosis, is well known in the younger age groups.[2,3] The most authoritative authors on acoustic neuroma,[1,3,4] however, emphasize the late age of onset of unilateral acoustic tumors unassociated with other pathological stigmata. Cushing[1] states that " . . . the symptoms of an acoustic tumor rarely occur before the third decade of life, . . . Hence one may be justified in the conclusion that a patient under 20 with a cerebellopontile-angle syndrome in all likelihood has a lesion other than an acoustic tumor." The case of unilateral acoustic nerve tumor presented here, however, proves to be a remarkable exception to that rule, for the age of onset was 6 years and the neuroma was removed and verified histologically when the child was $8\frac{1}{2}$ years old. Furthermore, this patient showed none of the associated stigmata of von Recklinghausen's disease, either by physical examination or family history. Some reports of unilateral acoustic neuroma occurring in the second decade have been presented[1,2,3] but none have been reported in the first decade of life.

Additional unusual features of this case include a normal spinal fluid protein and a massive destruction of the involved petrous pyramid (Fig. 1). These features did not alter the outline of therapeusis in this $8\frac{1}{2}$-year-old boy, but they made the probable histological diagnosis of his posterior fossa tumor an intriguing clinical problem.

CASE REPORT

This $8\frac{1}{2}$-year-old white male was admitted to the Boston Floating Hospital on June 10, 1951, and discharged on July 3, 1951.

Late in 1948, he had exhibited a mild transitory left facial weakness, which disappeared completely. In August 1949 there developed a sudden paresis of the left face which was persistent. Late in 1949, the patient noted the gradual onset of deafness in the left ear and he found he could no longer hear a watch tick in that ear. At this time the left eye was observed to close incompletely and the left side of the face seemed full. His symptoms were gradually progressive and in July 1950 he began to experience episodes of vomiting associated with vertigo. In April 1951 he began to deviate to the right while walking, and he tilted his head to the right. He also had trouble in keeping his balance when standing still.

Examination. There were no cutaneous or subcutaneous stigmata of von Recklinghausen's disease detected after thorough clinical investigation. Significant findings included no papilledema or signs of increased intracranial pressure. There was paresis of the left lateral rectus muscle and conjugate deviation to the right or left was poorly maintained. A slow bilateral horizontal nystagmus, with quick component in the direction of gaze, was also present. The corneal reflexes were normal. There was a severe left facial weakness, the forehead and both orbicularis groups being equally involved. Deafness on the left was of the nerve variety. There was no impairment of hearing on the right. The patient perceived painful stimuli in the left

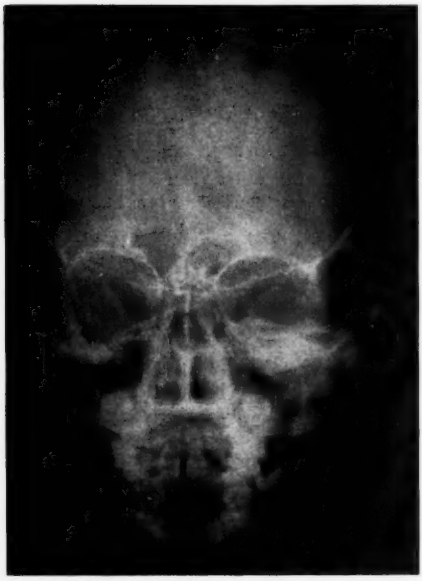

FIG. 1. Roentgenogram showing massive destruction of medial half of left petrous bone.

palate, and the tongue and uvula moved in midline. There was slight bilateral unsteadiness in the finger-to-nose test while the heel-to-knee test showed marked overshooting, especially on the left. There was no weakness or sensory deficit. Deep tendon reflexes were equal, though somewhat depressed, bilaterally. Plantars were extensor. The patient would fall either to the right or left in the Romberg position and he walked in a grossly wobbly fashion with his eyes closed.

X-rays of the skull showed a massive destruction of the medial half of the left petrous bone (Fig. 1). Lumbar puncture in the lateral recumbent position showed an initial pressure of 178 mm. with clear CSF. There were no cells; the colloidal gold curve was normal; total protein was 31 mg./100 cc.

Operation. On June 15, 1951, the left side of the posterior fossa was explored through an inverted U-shaped incision. The left cerebellopontine angle contained an encapsulated tumor roughly the size of a small lemon. It was situated quite laterally, eroding and infiltrating the petrous pyramid. The mass extended superiorly to the tentorial notch and seemed to compress the

FIG. 2. Photomicrograph of acoustic neuroma removed.

5th cranial nerve. A piece of the tumor was removed for rapid section diagnosis and was found to be acoustic neuroma. The tumor and its capsule were removed in a piecemeal fashion until only the rostral and lateral parts of the capsule remained. Separation of the capsule from the side of the brain stem was unusually simple for a tumor of this size. The anterior portion was then carefully dissected away from the 5th cranial nerve, leaving that structure intact. The lateral portion invading the bone was then completely removed. The 7th and 8th nerves could not be identified with certainty during the dissection.

Histological Diagnosis. Permanent sections were reviewed by Dr. Raymond D. Adams, and the classical picture of acoustic neuroma was again reported (Fig. 2).

Postoperative course was uneventful.

Examination 3 months later revealed an active boy who ate and slept well and who talked in an almost normal tone. Nightmares suffered preoperatively had disappeared. Left nerve deafness and complete left facial paralysis were the only deficits present. Tests of coordination and cerebellar function were within normal range, and the Romberg sign was negative.

DISCUSSION

The size and position of this tumor are of some interest. While Cushing drew attention to some unusual tumors 7 cm. in length, the ordinary large neuromas seldom reach this length and the tumor described in this report could certainly be considered as an example of a large tumor. The usual course of these tumors is prolonged and it is not unreasonable to believe that the inception of tumor growth preceded, by some time, the onset of symptoms in 1948 or 1949. This would place the date of inception of tumor growth before this child's 6th year of life.

The normal spinal fluid protein may be related to the extreme lateral position of the tumor. A good bit of tumor was found disrupting the petrous bone and a comparatively small amount of neuroma was seen to be protruding into the subarachnoid space of the angle. Tumor did not extend through the notch and a complete removal of the neoplasm was surprisingly easy.

CONCLUSION

An unusual case of unilateral acoustic neuroma is presented, occurring in an $8\frac{1}{2}$-year-old boy without stigmata of von Recklinghausen's disease.

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BENIGN ARACHNOID CYSTS OF THE POSTERIOR FOSSA

WILLIAM V. TROWBRIDGE, M.D., AND JOHN D. FRENCH, M.D.

Veterans Administration Hospital, Long Beach, California; and Departments of Surgery and Anatomy, University of California, Los Angeles School of Medicine

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Benign, monolocular cysts of the arachnoid in the posterior fossa are apparently quite rare. Sporadic reports of isolated cases of this type of lesion have appeared in the literature frequently under titles suggesting that their origin is due to inflammation.

The first clear description of such a lesion was found in a report by Craig,[2] in 1932, under the name of "chronic cystic arachnoiditis." In his Case I he described a cystic abnormality found in the midline of the posterior fossa, overlying the cerebellum and 4th ventricle. This case, however, was presented with 2 others, all of which were discussed as individual examples of a distinct, clinical entity. In one, a multilocular cyst, with fibrous and adhesive changes, was found in the posterior fossa of a 9-year-old child, following a prolonged, severe, pulmonary infection, complicated by signs of meningeal irritation. The other patient had a noncystic, posterior fossa arachnoiditis. The absence of cyst formation in one and the multilocular nature of the cyst in the other, especially with the evidence of acute inflammation, led us to consider the latter lesions dissimilar to the subject of this report.

Reference was made by Bucy[1] in 1946 to a similar cystic lesion in which a small tuft of choroid plexus was found attached to the cyst wall. This ectopic choroid plexus was held to be responsible for the fluid within the cyst, which, in compressing the vermis and the 4th ventricle, produced symptoms of intracranial hypertension.

A similar lesion was described in 1946 by Thompson,[7] who employed the term "cystic cerebellar arachnoiditis." In spite of this nomenclature, which implies an inflammatory origin, the etiology of the lesion was attributed to trauma sustained by the patient in a parachute jump.

In 1948 Kaplan[5] briefly reviewed the reports of Craig[2] and Thompson[7] and presented 2 similar cases of his own.

Much confusion exists in regard to the etiology of these lesions. In addition to the suggested role of trauma,[7] it has been implied that they are secondary to inflammation[2] and, also, that they are developmental anomalies.[5]

Review of the literature has failed to reveal reports of similar cases other than the 5 mentioned above. The rarity of this lesion, and the divergent opinion regarding its etiology, prompted the present report.

CASE REPORT

L.B.V.A.H., R#16935.

First Admission. J.H.B., a 25-year-old white male, was seen first in the out-patient department, in April 1950, with a primary complaint of headache. Approximately 1 month prior to admission, he had had a dental extraction under general anesthesia, following which severe, intermittent headaches developed. These were chiefly occipital in location, and on occasions were associated with mild dizziness and "numbness" of the entire left side of the body. The headaches would appear suddenly, but would ordinarily subside spontaneously after 5 to 30 minutes. At times they would be accompanied by nausea, and on rare occasions had been terminated by vomiting.

The paresthesias of the left side of the body were described as "like pins-and-needles." These appeared first in the foot and progressed slowly upward in a typical "sensory march" to involve the remainder of the left side of the body.

Past History. Approximately 5 years previously the patient had been "thrown about 15 feet" by the detonation of a torpedo striking the ship on which he was serving in the Navy. He remembered striking his head and injuring his neck, but he was not rendered unconscious.

Examination. The only neurologic abnormalities found were slight nystagmus on extreme lateral gaze in either direction and a "fullness" of the optic discs bilaterally.

Laboratory Tests. Lumbar puncture: the spinal fluid was under a pressure of 270 mm. of fluid; CSF cell count and chemistries were normal. An EEG on two occasions revealed non-focal (S-2) wave patterns.

Course. The symptoms subsided and the spinal fluid pressure fell to 160 mm. The patient was discharged, to be followed as a brain tumor suspect.

Second Admission. Three months later the patient returned, complaining that the headaches had become more frequent, more severe, and more persistent. Although their location remained predominantly suboccipital, on many occasions they had become generalized. Approximately 10 days prior to this admission, he had suffered an attack of severe nausea with vomiting. This was associated with a pronounced headache. Subsequently similar episodes had occurred, but he felt that they were becoming less severe. In the last few days there had been several episodes in which the patient described transient, complete loss of vision. These attacks lasted about 15 seconds and were preceded by a short period in which "everything turned gray." The previously described "tingling" sensations had continued to appear with the headaches, but had remained limited to the left side of the body.

For the last several weeks he had noted considerable "awkwardness" in movement of the extremities and in walking. This also occurred in episodes, sometimes involving only the legs, and sometimes the left leg and left arm only. There had been occasional "complete paralysis" of the right foot. These attacks, like all others, were transient.

Examination. The patient stood with the neck quite rigid and with the head tilted forward and to the left. Cerebration was slow but accurate. He was well-oriented in all spheres, and quite cooperative.

The right pupil was slightly larger than the left, but both pupils reacted briskly to light. There was bilateral papilledema of 2 D., with several small hemorrhages about the periphery of the discs. No field defects could be demonstrated. On looking to the left, there was fine nystagmus to the left; and on looking upward, there was fine vertical nystagmus, which, at times, appeared to move obliquely toward the left. The lower right facial muscles appeared to be somewhat weak. The remainder of the cranial nerves were intact.

There was a little unsteadiness in his movements, but at no time did he lose his balance. Some ataxia was present on heel-to-knee test bilaterally. There was mild ataxia on walking. His stance was wide, and the gait was somewhat staggering, but there was no tendency to fall to one side. There was no adiadokokinesis. No sensory abnormalities were found. Tendon reflexes were hypoactive throughout, with the exception of the ankle jerks, which appeared to be normal. All tendon reflexes were bilaterally symmetrical. Abdominal reflexes were active in all quadrants. No pathological reflexes could be elicited.

Skull films revealed minimal decalcification of the clinoids, but no other abnormalities were noted. Ventriculography disclosed symmetrically dilated lateral ventricles, and dilatation of the 3rd ventricle (Fig. 1).

Operation. Suboccipital craniectomy was performed through a vertical incision, the arch of the atlas being removed with the posterior part of the occipital plate. On opening the dura, a translucent, bluish, slightly fibrous cyst was seen lying exactly in the midline (Fig. 2). Below it could be seen the arachnoid of the medulla. The cyst, measuring approximately 2×3 cm., was opened, revealing the tonsils of the cerebellum to be pushed laterally on both sides. The base of the cyst extended inferiorly to the obex, its main bulk lying over the roof of the 4th ventricle. The walls were white, glistening and translucent, and through them could be seen the choroid plexus. Careful search was made for mural nodules in the wall of the cyst,

FIG. 1. Ventriculograms showing symmetrical dilatation of lateral ventricles, and dilated 3rd and 4th ventricles.

and none was found. After removing the cyst walls, the displaced—but uninvolved—velum of the 4th ventricle was opened, and there was no suggestion of a tumor mass in this region.

Postoperative course was uneventful, and the patient was totally symptom free when seen 11 months after operation.

Pathology. Hematoxylin and eosin preparations disclosed a folded cyst wall (Fig. 3). The lining of this cyst was composed of flattened arachnoid cell elements which had undergone

FIG. 2. Artist's illustration of appearance of arachnoid cyst at operation.

marked hyperplasia. Within the wall of the cyst there were many spaces and many thin-walled, dilated blood vessels. In areas, collections of arachnoid cells, suggesting hyperplasia, could be clearly seen. The wall of the cyst varied in thickness, and, in some areas, the outer portion of the wall was composed of hyalinized connective tissue. There was no evidence of infiltration with inflammatory cells, either around the vessels, or throughout the thickness of the cyst wall.

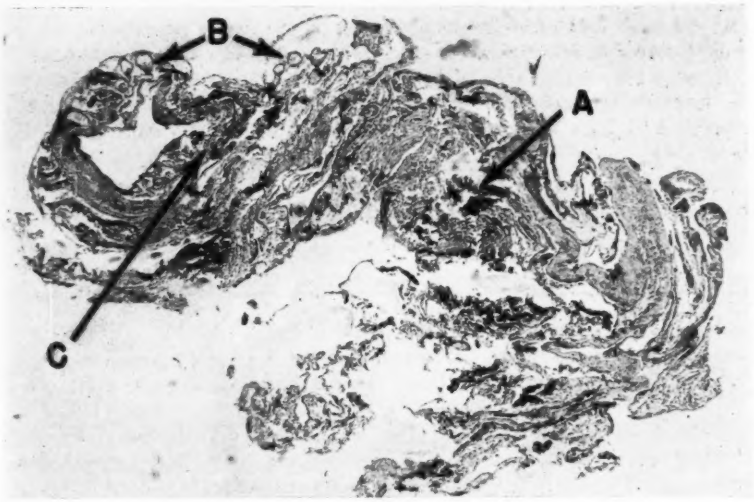

FIG. 3. Photomicrograph of cyst wall (hematoxylin and eosin, ×32). (A) Hyalinized connective tissue. (B) Thin-walled, dilated blood vessels. (C) Cluster of arachnoid cells.

DISCUSSION

It is immediately obvious that these cysts, acting as space-consuming lesions in the midline of the posterior fossa, precipitate symptoms primarily through obstruction of the 4th ventricle, and interference with the circulation of the cerebrospinal fluid. Previously reported cases, as well as the one reported here, presented symptoms and findings similar to those seen with midline cerebellar tumors. Specifically, they were characterized by signs of intermittent, severe, intracranial hypertension, and a paucity of localizing signs.

The intermittent nature of the symptoms, so strongly emphasized in almost all reports (Table 1), appears to be one of the most salient characteristics of these lesions. In Thompson's case,[7] changing the position of the head would relieve the severe headaches, which were likewise diminished by spinal drainage. It was his conviction that postural changes and lumbar puncture served to evacuate the cyst temporarily. Such a hypothesis must presuppose that there is, somewhere in the cyst wall, a hiatus through which drainage may be effected. Indeed, in the second case reported by Kaplan,[5] an opening was described at the lowermost portion of the cyst, through which fluid escaped from the 4th ventricle. In none of the other reports, however, is such a break in the continuity of the cyst wall mentioned. Moreover, in our patient, finger pressure on the delicate, tense, cyst wall produced

no evacuation of its contents. It would appear to be far more probable that the periodicity of attacks is due to a "ball-valve obstruction," as suggested for the similar phenomena observed with tumors of the 3rd ventricle.[3] By this means, such a lesion could produce obstruction, elevating cerebrospinal fluid pressure to a point where the channel is again opened, and the obstruction temporarily relieved. As with tumors of the 3rd ventricle, the periods between attacks gradually shorten, until the obstruction finally becomes complete.

The dizziness and paresthesias in our case are again reminiscent of the 3rd ventricle tumors, with which such symptoms appear to be quite common.[3] Moreover, Dandy[3] described a case of tumor in the 3rd ventricle in which the patient suffered transient attacks of "complete loss of vision," apparently identical to those in our case. A logical explanation for these latter symptoms is wanting.

TABLE 1

Recorded data of 6 cases of posterior fossa arachnoid cyst

AUTHOR	AGE	SEX	DURATION OF SYMPTOMS PREOPERATIVELY	SYMPTOMS INTERMITTENT	TRAUMA	EVIDENCE OF INFECTION	PATHOLOGY
RUCY (11)	34	F	NOT MENTIONED	NOT MENTIONED	NOT MENTIONED	NONE MENTIONED	A BENIGN, NON-NEOPLASTIC, NON-INFLAMMATORY CYST OF THE LEPTOMENINX ... ATTACHED TO A PART OF THE WALL AS A SMALL TUFT OF CHOROID PLEXUS
CRAIG (12) CASE #1	23	F	11 YEARS	+ + + +	NONE MENTIONED	DESCRIBED INFLAMMATORY CYST AT OPERATION	NO MICROSCOPIC PATHOLOGY REPORTED
KAPLAN (13) CASE #1	32	M	5 6 YEARS	+ + + +	NONE	NONE	... CELLS SIMULATING ARACHNOID ... TWO LAYERS OF CELLULAR GROUPS BETWEEN WHICH THERE WERE FIBROUS PARTITIONS AND THIN-WALLED BLOOD VESSELS ... NO INFLAMMATORY OR NEOPLASTIC ELEMENTS
KAPLAN (13) CASE #2	17	F	5 MONTHS	+ + + +	NONE	NONE	... DENSE HYALINIZED CONNECTIVE TISSUE AND A FEW BLOOD VESSELS ... ALSO A FEW DEEPLY STAINED OVAL AND ROUND NUCLEI ... SOME IDENTIFIED AS LYMPHOCYTES, OTHERS APPEARING AS FIBROBLASTS
THOMPSON (17)	23	M	25 MONTHS	+ + + +	NO DIRECT TRAUMA TO HEAD	NONE MENTIONED	... THE CYST WALL CONSISTED OF THIN FIBROUS TISSUE ... SHOWING INVASION OF SMALL ROUND CELLS WITH AN OCCASIONAL POLYMORPHONUCLEAR LEUKOCYTE
TROWBRIDGE & FRENCH	25	M	4 MONTHS	+ + + +	NONE	NONE	FOLDED ARACHNOIDAL CELL ELEMENTS ... MARKEDLY HYPERPLASTIC THIN-WALLED, DILATED BLOOD VESSELS ... NO EVIDENCE OF INFLAMMATORY CELLULAR INFILTRATION

A tabular review of the available data on these lesions (Table 1) reveals a number of striking similarities. In spite of the small series, it is quite remarkable that the age distribution is in the 3rd and 4th decades only. It is tempting to suggest, in view of the histologic nature of the cyst wall (Fig. 3), that the walls of these cysts are actively secretory, producing the fluid within the cyst. Such fluid production would probably be quite slow, allowing the nuances of osmotic and hydrostatic equilibrium to maintain a relatively stable relationship between the fluid in the cyst and the liquor in the surrounding cisterna cerebellomedullaris. In this manner, the cyst might slowly enlarge, over a number of years, to a point where equilibrium could be greatly disturbed and eventually abolished by the intermittent obstructions to the cerebrospinal fluid pathway. In support of this suggestion is the fact that similarly obstructing lesions, the colloid cysts of the 3rd ventricle, rarely become clinically manifest before the 20th year.[3]

The suggested etiologic role of trauma[7] becomes quite questionable when it

deserves no mention in the meticulous clinical histories (Table 1) of three reports.[1,2,5] As Kaplan[5] has pointed out, the trauma sustained by Thompson's patient[7] was minimal, and, moreover, was not delivered to the head. In our case, the patient suffered trauma to the head from a blast concussion 5 years prior to the onset of clinical symptoms. This can hardly be taken to be significant. It would appear, from the evidence at hand, that a hypothesis offering trauma as the responsible agent for these lesions would be quite tenuous.

Adhesive, scarring lesions of the leptomeninges, secondary to inflammation, are well known.[4] First glance separates the pathology under discussion into a totally separate group. All the descriptions encountered, in the present review, strictly avoid terminology suggesting advanced scar formation. Emphasis is directed toward picturing a thin-walled, velamentous cyst, not adhesive to the overlying dura, and with no described inflammatory reaction in the surrounding leptomeninx. The illustrations presented [1,2,5,7] support the descriptions. Craig,[2] who has thus far been alone in suggesting an inflammatory origin of these cysts, apparently bases his belief on the gross appearance of the lesion. Unfortunately, no histological description of the cyst wall was included in his report. Review of the collected reports (Table 1) is marked by the conspicuous absence of reference to clinical signs of inflammation, either general or of the central nervous system, in association with this abnormality. The microscopic reports accompanying the cases of Kaplan,[5] as well as the preparations in our own case (Fig. 3), show none of the characteristics of either acute or chronic inflammatory cellular infiltration. It is our belief that inflammation plays no part in the origin of these cysts.

The belief that these abnormalities are congenital, as advanced by Bucy,[1] is very strongly supported by the presence of ectopic choroid plexus tissue in the cyst reported by him. Less well founded is the theory of Kaplan[5] that blocking of a few of the small openings in the foramen of Magendie stimulates the 4th ventricle to simulate an arachnoid villus, and attempt to invaginate into the occipital venous sinus.

The case described here revealed, in the microscopic sections of the cyst wall, structures strongly reminiscent of arachnoid cuffs (Fig. 3). As in the other pathological reports (Table 1), the wall contained many blood vessels, which were quite thin-walled. This picture is totally foreign to that of normal arachnoid, in which, though capillaries may be seen, there is normally no capillary bed.[6] The pronounced similarity of this picture to those of others[5,7] leads us to subscribe to a congenital origin for these lesions. The area in which they are found is in direct apposition to the embryologic site of invagination of the 4th ventricle choroid plexus. Visualization of the simplicity with which embryologic rests could become lodged in this region is anything but difficult. Rests such as these could easily develop into rudimentary secretory organs, or—as in one case[1]—into highly developed, mature, choroid plexus. The remaining condition for production of a cyst would be the incarceration of the ectopic tissue in such a manner that the fluid produced could not circulate freely. The consistent midline position of such abnormalities is further support of their congenital origin.

Worthy of note is the fact, that, in all of these patients, distress was immediately and—to all appearances—permanently relieved by removal of the cyst. Although none of these lesions was correctly diagnosed, or even suspected, pre-operatively, they should be counted among the favorable operative lesions of the posterior fossa.

There appears to be no group of findings suggestive of a diagnostic syndrome specific for arachnoid cysts of the posterior fossa. Numerous features, however, segregate these lesions from inflammatory arachnoiditis in the posterior fossa, and they are felt to constitute a distinct, pathological entity.

Appreciation is expressed to Charles Bridgman, Timothy Dodge and Thomas Masterson for their help in preparing the illustrations.

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COLLOID CYST OF THE FOURTH VENTRICLE

REPORT OF A CASE OF TWO COLLOID CYSTS OF THE FOURTH VENTRICLE

Dwight Parkinson, M.D.,* and A. E. Childe, M.D.†
Winnipeg, Manitoba

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The term, "colloid cyst," to the neurosurgeon invariably connotes the single cystic mass occurring always at the anterior portion of the 3rd ventricle adjacent to the foramen of Monro. The predilection of these cysts for this location and their absence from other portions of the ventricular system have been explained on the basis that they arise from the embryonic paraphysis.[1,5,7,12,15] The paraphysis is an epithelial outpouching with numerous tubules from the telencephalic part of the roof of the 3rd ventricle just in front of the velum transversum. This structure is reportedly common to all vertebrates but not found beyond the 32 mm. stage in human embryos.[1]

These colloid cysts are commonly referred to as "paraphysial cysts," although Dandy, who did most to bring them to medical attention, preferred the descriptive term, "colloid cyst," without reference to their possible origin.

Various reasons have been offered for believing that these cysts arise from the paraphysis—the presence of numerous rudimentary tubules in the cyst wall,[12] the presence of ciliated epithelium and the location of the cysts.

Not all reported cases have been similar nor have they necessarily all evidenced the above criteria. The lining has varied from fairly flat epithelium[9] to single-layered cuboidal[2,10,14] to columnar ciliated[3,4,8] epithelium. Perhaps some of these

* 428 Medical Arts Bldg., Winnipeg, Manitoba.
† 101 Medical Arts Bldg., Winnipeg, Manitoba.

are not true paraphysial cysts but more likely the amount of distention in each case alters the architecture of the lining epithelium.

The amount of the cyst wall that has been adherent to and covered by the choroid plexus has varied considerably in different cases also.

One cyst was apparently in the posterior part of the 3rd ventricle.[4]

The following case is unusual in two respects. There were two colloid cysts and they were both in the 4th ventricle. The authors are not aware of any previous cases of colloid cyst of the 4th ventricle.[6]

CASE REPORT

M.L., a male aged 28, was considered well until the latter part of June 1951, 8 weeks before admission. At that time he noted a sensation as though ants were crawling over the skin of his left occiput. Within the next day or two he began to stagger and notice blurring of his vision. In the latter part of July, he began to vomit and he was admitted to another hospital where he was investigated for disturbance of the intestinal tract until the time of admission to the Winnipeg General Hospital, Aug. 24, 1951. Headache was never a complaint, but the vomication persisted until his operation.

Examination. He was a well built but haggard-appearing young male, rather reluctant to be disturbed from his curled-up position in bed. He walked with an ataxic gait. There was a fine, rapid nystagmus on lateral deviation, most marked to the right. There were bilateral acutely choked discs.

On Aug. 28, 1951, under local anaesthesia, ventriculography was performed with recovery of 30 cc. of clear CSF. There was free communication between the two lateral ventricles. Subsequent roentgenograms revealed a moderate degree of symmetrical dilatation of both lateral ventricles and of the 3rd ventricle. In spite of adequate manipulation of the head, the aqueduct of Sylvius was visualized only in its proximal 5 mm. This portion of the aqueduct was dilated, measuring 3.5 mm. in diameter. A small quantity of oxygen had passed beyond this point and it partially filled a considerably enlarged 4th ventricle. The basal cisterns were not outlined. These findings were interpreted as indicating a lesion that was obstructing the exit of CSF from the 4th ventricle and that was also extending up into and partially obstructing the aqueduct (Figs. 1, 2, and 3).

Operation. A midline cerebellar craniotomy was performed the same morning. The tonsils both extended down to the inferior edge of the arch of the atlas. As the tonsils were separated there was seen protruding through the foramen of Magendie a smooth-walled, fluctuant, blue-gray mass resembling a nasal polyp in appearance and consistency. This was gently teased out and delivered; it had no apparent attachment although the cyst wall broke in the process, releasing a homogeneous clear gelatinous fluid. When reexpanded this cyst measured 1.5 cm. in diameter. On reexamining the foramen another similar but smaller projection was seen to have taken the place of the first. This was removed easily without rupture and measured about 1 cm. in diameter. There was no bleeding associated with the removal and there was no irregularity on the surface of either cyst that could have represented a point of attachment. There was a free gush of CSF after the second cyst was removed. However, feeling that if there were two there might be more, the vermis was split and the entire surface of the 4th ventricle inspected. There were no more cysts visible nor was there any evidence of a point of attachment, although the midline of the roof was of course traumatized in the exposure. The aqueduct allowed passage of a #8 French catheter into the 3rd ventricle. The wound was closed.

Course. The patient made an uneventful recovery. He was last seen on Dec. 6, 1951 at which time he had gained 25 lbs. and had been working as a laborer in the woods since his discharge from the hospital. He was completely free of his intracranial symptoms. His nystagmus and papilloedema had disappeared.

FIG. 1. Lateral ventriculogram showing dilatation of the lateral and 3rd ventricles and also of the proximal 5 mm. of the aqueduct of Sylvius (arrow).

FIG. 2. Brow down, lateral ventriculogram made following manipulation of the head. There is now shown to be some gas in the posterior part of the 4th ventricle, which is enlarged considerably posteriorly (arrow).

FIG. 3. P.A. ventriculogram showing dilated lateral and 3rd ventricles as well as the dilated 4th ventricle (arrows), which is situated in the midline.

Microscopic Examination. The cyst wall was lined by columnar ciliated epithelium with an enveloping narrow layer of fibrous stroma (Figs. 4 and 5).

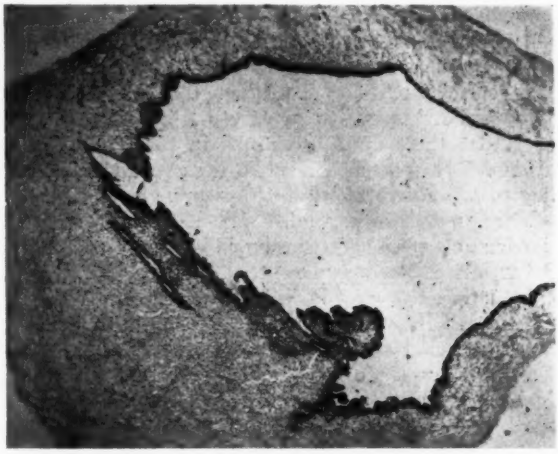

FIG. 4. Collapsed portion of cyst wall (×40) showing lining membrane in folds. In the upper left portion several small epithelial-lined tubules are visible at quite a distance from the lining of the main cavity. Some larger ones can be seen in the left mid-portion. (W.G.H. Path. #5672/51).

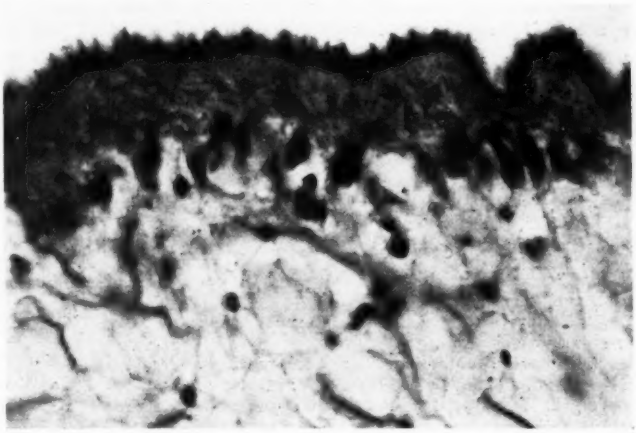

FIG. 5. High magnification (×1000) of inner surface of cyst wall showing the ciliated columnar epithelial lining and the underlying loose stroma.

DISCUSSION

There can be little doubt that grossly and microscopically these two cysts are identical with the typical colloid cyst of the 3rd ventricle. The question at hand is how did they get in the 4th ventricle. There are two possibilities: either they

originated there from the ependymal lining or they migrated through the aqueduct after having been detached from the 3rd ventricle. Neither one could have navigated the aqueduct in their present size. It is possible that they came through in a smaller size and then grew, nourished as free bodies in the fluid of the 4th ventricle. They were obviously being nourished sufficiently to prevent necrosis as apparent free bodies in the 4th ventricle, whether originating there or not. The ventriculogram is best explained by one cyst partially obstructing the distal aqueduct and the other obstructing the foramen of Magendie.

The possibility that these cysts originated in the 4th ventricle seems more likely to the authors. If they washed through the aqueduct in their infancy there should be nothing to prevent them washing on through the foramen of Magendie to lodge in the cisterna magna or beyond.

Just which portion of the 4th ventricle should be suspected of giving birth to the cysts can only be surmised. The argument that all colloid cysts are formed by the embryonic paraphysis does not seem logical. The ciliated lining of these cysts does not necessarily mean that they can arise only from the paraphysis. This structure and the remaining ependymal lining all have a common origin from the embryonic ectoderm. The cystic masses[11] covered with epithelium that resembles choroid plexus, probably begin as papillomata whose supporting stromal core undergoes cystic degeneration. These may be related but are certainly not the same as the cysts in this report which are lined, not covered, with epithelium, which epithelium is embryonic in nature.

SUMMARY

A case of two colloid cysts of the 4th ventricle is presented, believed to be the first such report. The possibilities of origin are discussed.

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GLIOMATOSIS CEREBRI

N. MALAMUD, M.D., B. L. WISE, M.D., AND O. W. JONES, JR., M.D.

Laboratory of Neuropathology, The Langley Porter Clinic, and Division of Neurological Surgery, University of California Hospital and Franklin Hospital, San Francisco, California

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In 1938, 3 cases were reported by Nevin[6] under the title of "Gliomatosis Cerebri." His first patient was a 23-year-old woman who had progressive symptoms of failing memory, emotional deterioration, petit mal seizures, papilledema, and headaches over a period of 10 months; she died shortly after a lumbar puncture and ventriculography. The second patient was a 27-year-old man who had convulsions, impairment of memory, and headaches of $2\frac{1}{2}$ years' duration; he died a year after a decompression operation. The third case concerned a 54-year-old woman with a history of lifelong convulsive seizures and pigmentation of the skin characteristic of von Recklinghausen's disease, who in the last 4 years of her life showed progressive mental deterioration, and towards the end, a right hemiplegia, papilledema and stupor; she died shortly following hospitalization. In all 3 cases the autopsy disclosed macroscopically only slight enlargement and discoloration of various parts of the brain tissue, but microscopically there was a striking diffuse overgrowth of neuroglial cells in all stages of development throughout wide areas of the cerebral hemispheres with little or no tendency to local tumor growth. Nevin compared his cases with those reported previously under various designations by Hildebrandt,[4] Landau,[5] Cassirer and Lewy,[1] Schwartz and Klauer,[9] Foerster and Gagel,[3] and von Sántha.[7] To these may be added more recent reports by Scheinker and Evans.[8] Because of the diagnostic difficulties presented by this condition and because of its theoretical interest, the following case is here reported.

REPORT OF CASE

History. A.S., a white male, aged 17 years, began to complain of persistent diplopia and occasional attacks of nausea and vomiting in the spring of 1948. He was first seen by a physician in June 1948, at which time a paralysis of the right medial rectus muscle was the only finding. He was treated with eye-muscle exercises. By September 8, 1948 his condition had progressed to an almost complete right external ophthalmoplegia. There was also a mild right exophthalmos and mydriasis with normal pupillary reactions. On December 14, he was found to have bilateral hemorrhagic papilledema of 3D and was therefore admitted to the hospital.

Examination revealed, in addition to the right-sided ocular signs and bilateral papilledema, a fine horizontal nystagmus on gaze to the left, mild left supranuclear facial paresis, and increased deep tendon reflexes on the left. Two days following admission, the patient had a generalized convulsive seizure. Laboratory studies were entirely negative. Ventriculogram revealed a questionable slight shift to the left without deformity, no air having entered

the right ventricle. A right carotid arteriogram showed a normal arterial system. A lumbar puncture disclosed a pressure of 300 mm. of water and the fluid was entirely negative.

Course. Transient weakness of the left superior rectus and vertical nystagmus appeared. The patient was discharged from the hospital and followed periodically. During the next 4 months there was progressive decrease in visual acuity with increasing pallor of the optic discs, and slight impairment of memory for recent events.

2nd Admission, April 3, 1949. A repeat ventriculogram showed slight bilateral enlargement of the lateral ventricles and slight displacement to the left and upwards.

It was felt that the patient had an intrinsic tumor of the brain stem. A right subtemporal decompression was performed on April 15, followed by a course of deep x-ray therapy, consisting of 2100 r. (in air) to each of three cranial fields and 1500 r. to a fourth field.

Course. The patient showed marked remission of his symptoms for about 1 year. The papilledema completely subsided and the visual acuity became normal. The right ocular palsies showed marked improvement but the nystagmus and reflex changes on the left side persisted. His memory improved and he went back to school.

Re-examination in April 1950, however, revealed decreased auditory acuity and peripheral facial paresis on the left side.

In September, generalized convulsions developed, and the following signs were elicited: bilateral limitation of inward and upward gaze, horizontal nystagmus on looking to the left, marked left-sided auditory impairment, marked left peripheral facial paralysis, hypalgesia in the distribution of the left trigeminal nerve, deviation of the uvula to the right, and hyperactivity of the deep tendon reflexes on the left with depressed abdominal skin reflexes and an equivocal Babinski sign on the left. He was consequently re-admitted to the hospital.

3rd Admission, Oct. 12, 1950. He showed mental blunting and a horizontal nystagmus on gaze, both to the right and left. Ventriculography now revealed the ventricles to be of normal size and there was no displacement. The subtemporal decompression was full, and he was given another course of x-ray treatments, consisting of 2200 r. to each of four fields, and was discharged.

Course. The trigeminal hypalgesia disappeared and there was slight general improvement for several months followed by relapse. In March and April of 1951, additional signs were noted: marked impairment of memory, slurring of speech, mild ataxia of body and extremities, and episodes of mental confusion associated with clonic movements of the right upper extremity preceded by an aura of peculiar odors.

4th Admission, April 27, 1951. At this time he was described as lethargic. The subtemporal decompression was bulging due to increased pressure. The optic discs were pale with questionable early elevation. There was moderate paresis of the medial and lateral recti on the left, and mild paresis of the medial rectus and inferior oblique on the right; the right eye turned up and out on upward gaze. Vertical and horizontal nystagmus were present. There was a left peripheral facial paresis. There was no useful hearing on the left. Deep tendon reflexes were equally hyperactive. There were mild paresis and ataxia of the left lower extremity and hypalgesia of the anterolateral surface of the right thigh.

Further x-ray therapy was instituted, consisting of 1100 r. to each of two cranial fields and 2400 r. to the lumbosacral spine.

On May 28, the patient became stuporous and had frequent Jacksonian seizures involving the right upper extremity followed by right hemiparesis and aphasia. On June 10, he manifested hematemesis and melena, and died on June 16, 1951, approximately 3 years following the onset of his illness.

Autopsy. The only significant findings in the internal organs were petechial hemorrhages in the mucosa of the lower end of the esophagus, stomach, and colon.

Central Nervous System: Macroscopic Observations. The brain was abnormally heavy, and gyri were moderately flattened, and there was slight bulging in the temporoparietal region of the right hemisphere (Fig. 1A). Sections disclosed slight increase in consistency of the tissue, poor demarcation of the gray and white matter in some areas, and a small focus of necrosis in the white matter adjacent to the tip of the left posterior horn (Fig. 1C). There were, how-

ever, no signs of localized tumor growth nor any changes in the ventricular system. The brain stem, cerebellum, and spinal cord were not remarkable with the exception of a small oval-shaped grayish-white, firm nodule intimately attached to the conus medullaris (Fig. 1B).

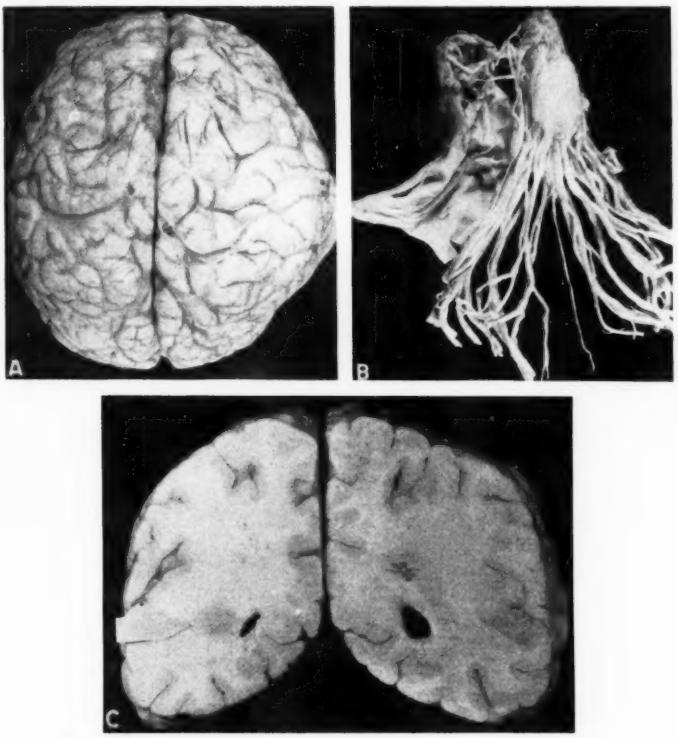

FIG. 1. (A) External appearance of brain showing flattening of gyri and bulging on the right side at site of temporal decompression. (B) Tumor nodule attached to conus medullaris and cauda equina. (C) Section through occipital lobes showing poor outlines of grey and white matter and a focus of necrosis on the left side (arrow).

Microscopic observations revealed a universal infiltration of the central nervous system by neuroglial elements. In sections taken from various parts of the cerebral cortex, a most striking picture was the formation of a broad zone of glial nuclei and fibers in the outer part of the molecular layer. Because of its uneven development, it gave the surface of the cortex a scalloped appearance. In its composition it varied from areas that contained aggregates of small nuclei embedded in a slightly fibrillary matrix (Fig. 2A) up to others that consisted of a dense network of glial fibers emanating from underlying proliferating astrocytes (Fig. 2B). Not infrequently, this marginal gliosis extended through the pial limiting membrane into the leptomeninges (Fig. 2C), where it partially obliterated the sulci.

Beneath the marginal change, the cerebral cortex showed widespread proliferation of glial elements (Fig. 3A). These showed predilection for a perineuronal and perivascular arrangement, and obscured but did not appreciably disturb the normal cytoarchitecture. Thus many of the neurons were surrounded by clumps of three to six nuclei (Fig. 3B), but surprisingly

few of them showed pathologic changes and their numbers were not definitely diminished. The tangential fibers in myelin stains were, however, more distinctly altered. Many of the cortical blood vessels were encircled by dense cuffs of similar glial elements, which, however, did not break into the perivascular spaces. The nuclei of the infiltrating cells varied from rod to oval to transitional forms and contained moderate amounts of chromatin. The cytoplasm failed to stain with most methods. However, with Mallory's phosphotungstic acid hematoxy-

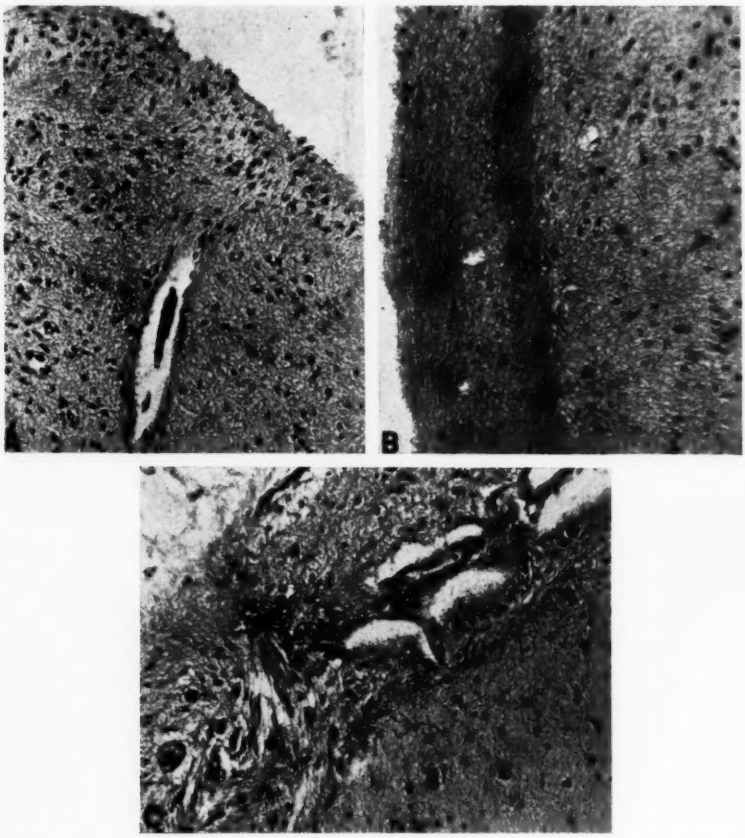

FIG. 2. Changes on surface of the cerebral cortex. (A) Glial nuclei embedded within slight fibrillary matrix. (B) Dense marginal gliosis. (C) Infiltration of the leptomeninges by glial tissue. ×100, Holzer stain.

lin, many of these elements had faintly bi- or unipolar processes, while some were definite astrocytes with stellate bodies and one or two branching processes encircling the ganglion cells or radiating to neighboring blood vessels. In Cajal's gold sublimate and Hortega's silver carbonate preparations only the few astrocytes stained. Although the immature glial elements predominated, there were some cortical areas that were composed entirely of astrocytes, resembling a diffuse astrocytoma (Fig. 3C).

There was no definite localization of the process, but the temporoparietal cortex was somewhat more involved than the frontal and more so on the right side, while the occipital cortex was severely involved on both sides. The greater part of the cerebral white matter showed only mild involvement, resulting in a sharp contrast between it and the infiltrated cortex.

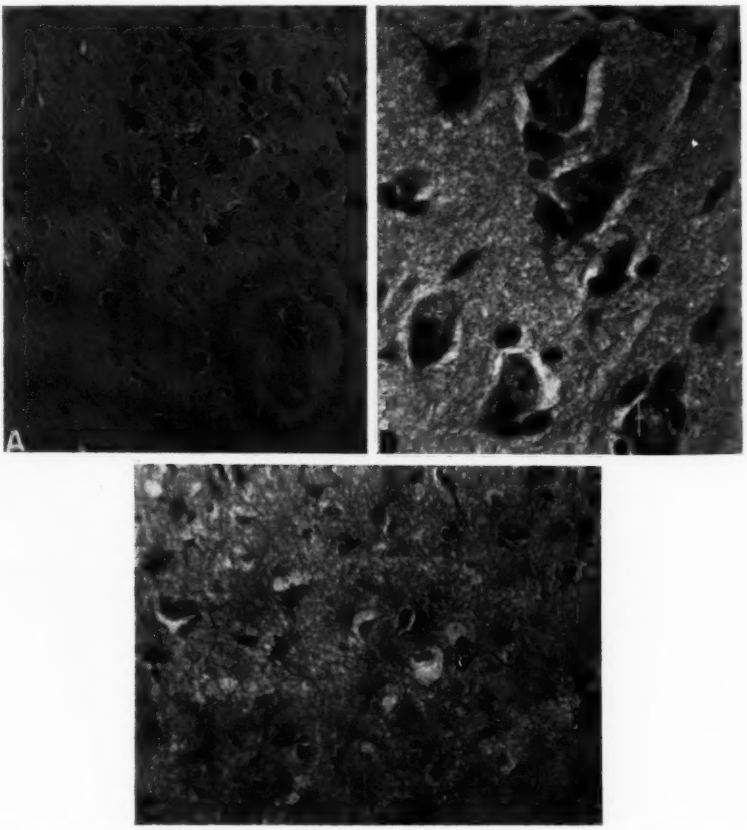

FIG. 3. Cerebral cortex showing perineuronal satellitosis by primitive glial elements. (A) ×100. (B) ×460, Mallory's phosphotungstic acid hematoxylin stain. Note single astrocyte in center of field. (C) Cerebral cortex infiltrated exclusively by astrocytes. ×100, Holzer stain.

However, in the white matter of the occipital lobes, the Weigert preparations (Fig. 4A) showed a striking subcortical diffuse demyelinization and a relative preservation of the U fibers. Here the Holzer preparations showed a diffuse astrocytosis of the white matter (Fig. 4B), and in the grossly observed necrotic focus on the left, there were proliferated and thrombosed blood vessels accounting for the areas of necrosis. There was mild to moderate increase in glial fibers throughout the subependymal regions of the ventricles.

The basal ganglia were only moderately involved, more so the caudate nucleus than either the putamen or globus pallidus, while only minimal changes were noted in the internal capsules. On the other hand, the thalamus was severely and bilaterally involved, showing

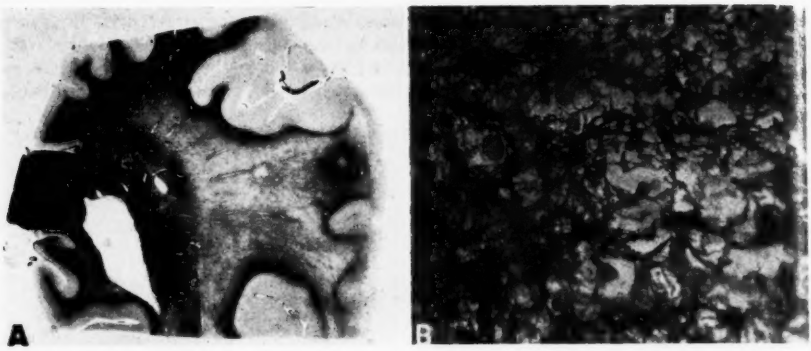

FIG. 4. Left occipital lobe. (A) Diffuse demyelination of white matter. Natural size, Weigert stain. (B) Dense proliferation of astrocytes and glial fibers in demyelinated areas. ×100, Holzer stain.

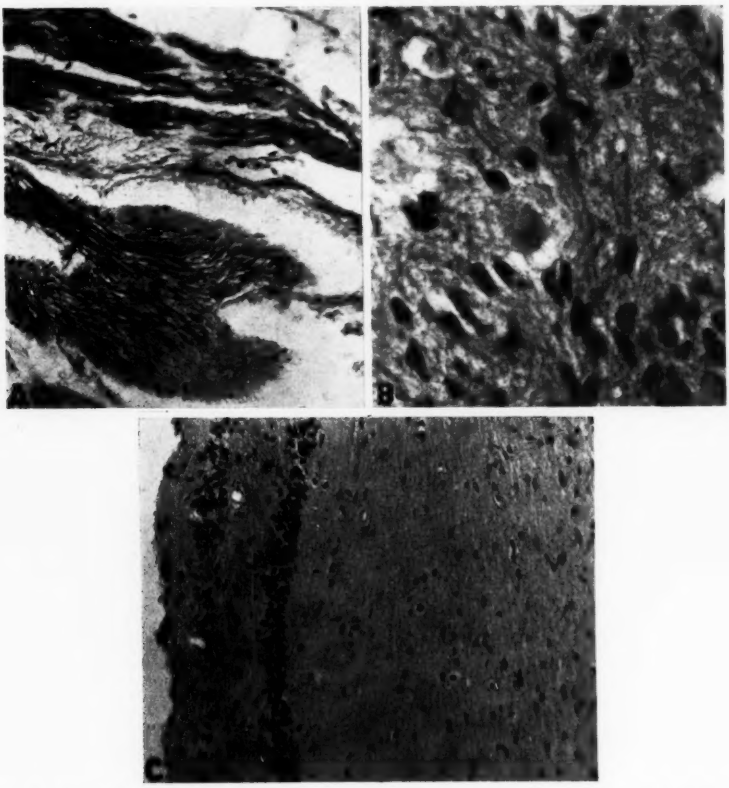

FIG. 5. (A) Root of facial nerve showing glial infiltration. ×100. (B) Tegmentum of pons showing perineuronal infiltration by polar spongioblasts and occasional astrocyte. ×460. (C) Surface of cerebellum showing marginal glial infiltration. ×100, Mallory's phosphotungstic acid hematoxylin stain

abundant and diffuse infiltration of the gray matter, more particularly of the dorsomedial nuclei, but relative preservation of the intervening laminae of white matter. There was moderate infiltration in the hypothalamus, subthalamus, and optic chiasm.

The midbrain showed severe and bilateral infiltration of the tectum, the nuclei of the 3rd and 4th cranial nerves, and much less involvement of the substantia nigra and the red

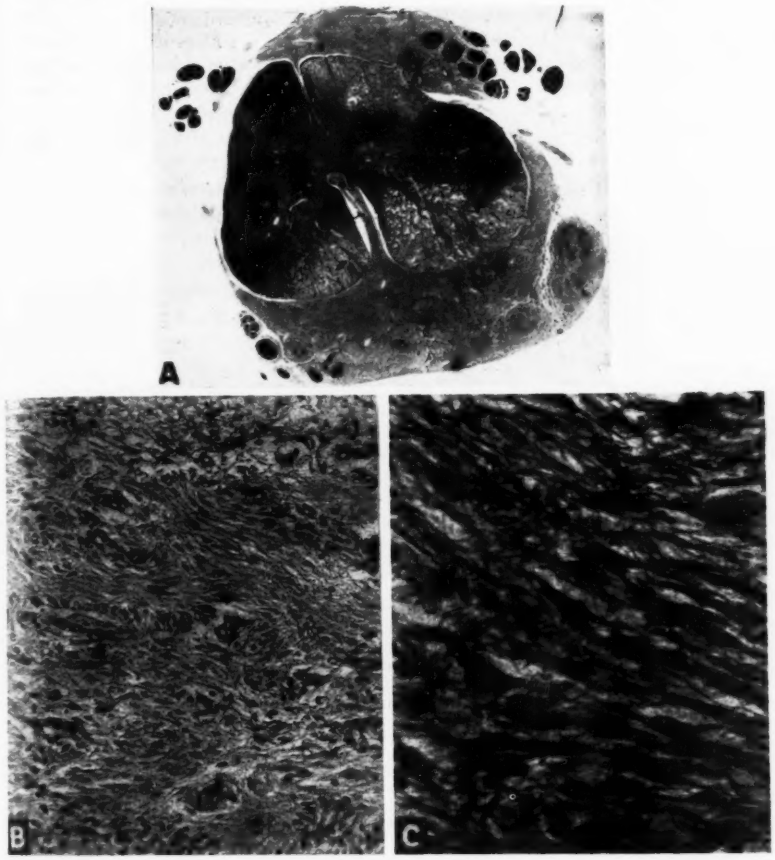

FIG. 6. Section through tumor nodule in region of conus medullaris. (A) Infiltration of leptomeninges and necrosis of spinal cord, in neighborhood of nerve roots. ×4, Weil stain. (B) Infiltration of leptomeninges by polar spongioblasts. ×100. (C) ×460, Heidenhain's aniline blue stain (Azan method).

nucleus. The tegmentum of the pons was more severely affected than the basilar portion and the cranial nuclei of the medulla more than the inferior olives and pyramids. A marginal gliosis surrounded the brain stem, which tended to invade the meninges and roots particularly of the 5th, 7th, and 8th cranial nerves (Fig. 5A). Throughout the thalamus, basal ganglia, and brain stem the infiltrating cells varied, as in the cortex, from immature forms to astrocytes (Fig. 5B), the latter rarely predominating.

In the cerebellum, the most conspicuous change was also a marginal gliosis occurring most frequently as a dense, double layer of glial elements interspersed with fibers (Fig. 5C). Be-

neath this, there was regional infiltration of the molecular and Purkinje layers, the Purkinje cells having almost completely disappeared in some areas. The dentate nucleus was moderately involved, but not the white matter of the cerebellum.

The spinal cord at various levels revealed only a mild to moderate marginal gliosis. However, in the grossly described area of tumefaction in the conus, there was an extensive invasion of the leptomeninges by glial tissue, particularly in the vicinity of the ventral and dorsal roots (Fig. 6A). This consisted of interlacing bundles of elongated cells and nuclei, many of which appeared to have uni- or bipolar processes, lying in a stroma of dense reticulin and scant glial fibers (Figs. 6B, 6C). In areas of most intense meningeal involvement, there was marked pressure necrosis of the anterior columns and moderate necrosis of the dorsal columns of the cord.

COMMENT

Our case resembled in all essentials those reported by Nevin and the other authors mentioned above. Clinically, there was the same evidence of a diffuse and progressive disease of the central nervous system accompanied by signs of increased intracranial pressure. The unique features in our case were: (1) the greater variability of the symptoms from initial brain stem to ultimate cerebral, cerebellar, and conus signs, and (2) the favorable response, even though for a limited time, to decompressive and x-ray therapy. All these manifestations strongly suggested a neoplastic disorder. The diagnostic difficulties, however, stemmed from the lack of localization of the process and its constant fluctuations as it engulfed larger and different areas of the nervous system. Pathologically too, the changes in our case were similar to those previously reported, viz., widespread infiltration of the growth throughout the central nervous system, a tendency to subpial, perivascular, and perineuronal distribution, variable structure of the neuroglial cells from predominant immature and polar spongioblasts to infrequent mature astrocytes, and the gross and microscopic preservation of the underlying nervous structures.

This condition has been variously designated in the literature as gliomatosis cerebri (Nevin[6]), blastomatous type of diffuse sclerosis (Cassirer and Lewy[1]), central diffuse Schwannosis (Foerster[3]), diffuse cerebral glioblastosis (Scheinker and Evans[8]), etc. The majority of authors regarded the condition as a developmental anomaly of the neuroglia rather than as a true neoplasm. Nevin based this view on the apparent simultaneous growth in different areas, the intactness of the normal structures, the great variations in the type of neuroglial cells and the differences in manner of growth in grey and white matter. He compared gliomatosis cerebri with generalized neurofibromatosis of von Recklinghausen, and found confirmation of the similar blastomatous character in their coexistence in one of his cases and in the case reported by Foerster. On the other hand, he compared his cases with the polar spongioblastomas of the optic chiasm and brain stem and with the diffuse astrocytomas described by Elvidge, Penfield and Cone,[2] suggesting that all of these are essentially blastomatous disorders.

It seems to us, however, that the improbability of this viewpoint is already inherent in such broad generalizations, particularly when the fundamental nature of these various growths remains unknown. In our opinion, the neoplastic basis of cases of gliomatosis cerebri is already evident in their onset in adult life, their rapidly progressive course, the signs of increased intracranial pressure, and their partial response to decompression and x-ray treatment. The occasional occurrence of such tumors in cases of von Recklinghausen's disease does not prove their inci-

table relationship any more than the occurrence of polar spongioblastomas or meningiomas in that disease.

On the other hand, there is undoubtedly a close morphologic resemblance between diffuse gliomatosis and polar spongioblastoma. In both, infiltration of neoplastic cells around relatively preserved neurons and varying maturity of the cells are characteristic features. The only significant difference between the two types is the more widespread growth of diffuse gliomatosis. In our opinion, therefore, a term that would emphasize this relationship, such as diffuse polar spongioblastoma in cases of gliomatosis cerebri as opposed to localized polar spongioblastoma of the brain stem or optic chiasm, might be a more adequate designation. The comparison with astrocytoma diffusum is also warranted when, as in our case, areas possessing the characteristic structure of the latter tumor were noted. However, the relative infrequency of such changes would preclude the application of this diagnosis to the condition under consideration here.

SUMMARY

1. The clinical and pathologic features of a case of "gliomatosis cerebri" are reported.

2. It is suggested that this is a true tumor and may be classified with the polar spongioblastomas.

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BED ATTACHMENT FOR IMPROVED HEAD TRACTION

Charles F. Clayton, M.D.*
Fort Worth, Texas

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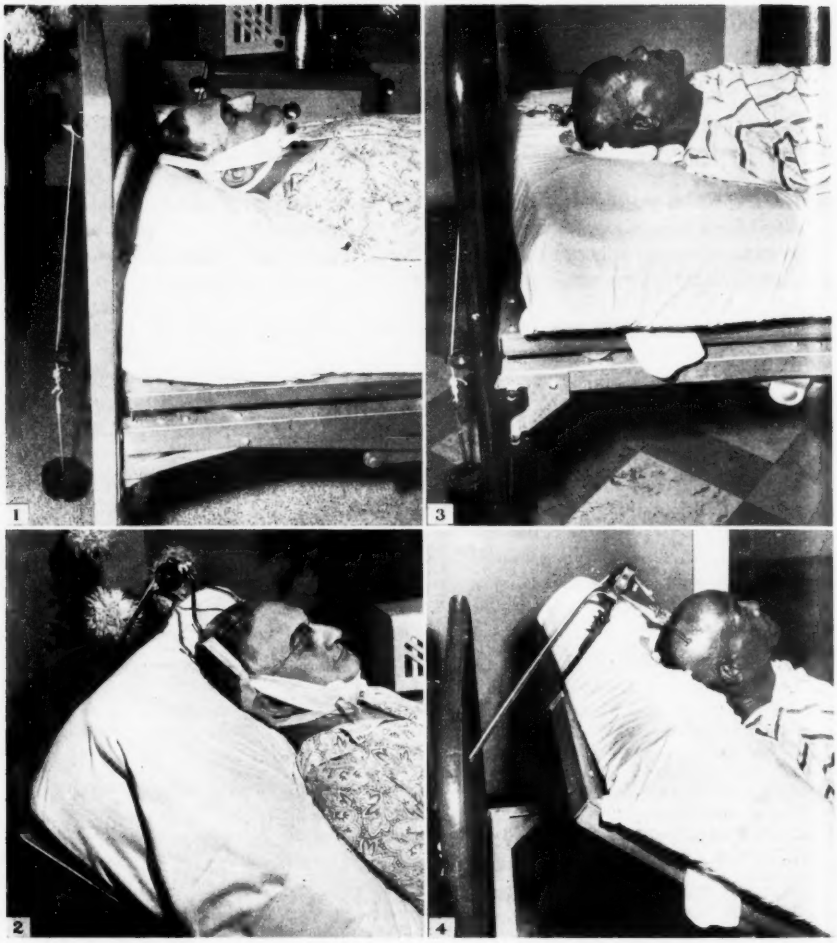
The efficiency of head traction as a therapeutic measure was immeasurably enhanced by the advent of tongs for application directly to the skull. This instrument makes possible the application of weight in excess of 30 pounds to the head,

* 1017 Medical Arts Bldg., Fort Worth 2, Texas.



with little or no discomfort, and also eliminates the necessity for interruption of the traction for feeding, shaving and other functions. As heretofore employed however, the measure entails considerable inconvenience for the wearer, who must of necessity spend the entire time while in traction completely supine, the traction pulley being fixedly attached to the head of the bed frame. This position renders feeding difficult, and such activities as reading and writing practically impossible.

In order to overcome these objections, and relieve the tedium of enduring head traction over long periods, the device herein described was designed. It consists of a metal bar, with perpendicular and diagonal segments, the former adjustable in height, with two pulleys and an end piece for attachment to the cross member of the elevating head section of the mattress frame. It permits the head section to be

elevated approximately 45° on most hospital beds, with no disturbance of the traction. Indeed, the elevated position tends to enhance the efficiency of the traction, by providing improved counter-traction. In this position the patient may take food without difficulty, and can read, and even write, by using a stand placed across the bed. The limits of his perception are expanded from a segment of room ceiling directly over his bed to the world about him, including the world of books, and he usually evinces his appreciation of his emancipation by insisting upon spending most of his waking hours in the elevated position.

The apparatus has been employed in a number of cases, with complete satisfaction. It may be used with either halter or skull traction, as shown in Figs. 1 to 4.*

* The apparatus is manufactured by Williams-Yeary Company, P.O. Box 7281, Fort Worth, Texas.

NOTICES

AMERICAN BOARD OF NEUROLOGICAL SURGERY

The following specialists were certified at a meeting of the American Board of Neurological Surgery in Chicago, Illinois, June 15–17, 1952.

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BOYER, FRANCIS CHRISTIAN 928 North Market Ave., Canton 2, Ohio
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FRESHWATER, DONALD B. 605 Commonwealth Ave., Boston 15, Mass.
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HAYES, GEORGE J. Medical Corps, U. S. Army
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TARKINGTON, JOSEPH 700 North Michigan Ave., Chicago 11, Ill.
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WILLIAMS, JOHN R. 626 Medical Arts Bldg., Grand Rapids 2, Mich.
ZOLL, JOHN G. 131 Linwood Ave., Buffalo 9, N. Y.

AMERICAN ELECTROENCEPHALOGRAPHIC SOCIETY

At the 6th Annual Meeting of the American Electroencephalographic Society in Atlantic City, N. J., on May 10, 1952, the following officers were elected: Dr. Robert B. Aird, San Francisco, President; Dr. Mary A. B. Brazier, Boston, President-Elect; Dr. John A. Abbott, Boston, Secretary; and Dr. Charles E. Henry, Hartford, Treasurer.

AMERICAN NEUROLOGICAL ASSOCIATION

At the 77th Annual Meeting of the American Neurological Association in Atlantic City, N. J., May 8 to 10, 1952, the following officers were elected: President,

Dr. Hans H. Reese; President-Elect, Dr. Roland P. Mackay; First Vice-President, Dr. Thomas K. Davis; Second Vice-President, Dr. James C. White; Secretary-Treasurer, Dr. H. Houston Merritt; and Assistant-Secretary, Dr. Charles Rupp.

HARVEY CUSHING SOCIETY

The 20th Annual Meeting of the Harvey Cushing Society was held in Victoria, B.C., June 5 to 7, 1952. The following officers were elected for the 1952–1953 term: Dr. William J. German, New Haven, President; Dr. Edgar A. Kahn, Ann Arbor, President-Elect; Dr. Eldridge Campbell, Albany, Vice-President; and Dr. David L. Reeves, Santa Barbara, Secretary-Treasurer. Dr. Louise Eisenhardt, New Haven, was elected Historian, and Dr. Paul C. Bucy, Chicago, was elected a member of the Executive Committee for terms of five years. Dr. A. Earl Walker, Baltimore, and Dr. Franc D. Ingraham, Boston, were appointed as representatives of the Society to the American Board of Neurological Surgery for terms of six years.

The next meeting of the Society will be held in Hollywood, Florida, April 22–25, 1953.

NEUROSURGICAL SOCIETY OF AMERICA

The 5th Annual Meeting of the Neurosurgical Society of America will be held at the Cloister, Sea Island, Georgia, September 18–20, 1952. The program includes discussions on the Treatment of Vascular Anomalies, Planned Hypotension in Surgery, Arteriography Versus Ventriculography in the Diagnosis of Brain Tumors, and the Present Status of Radio-Active Isotopes in Brain Tumor Diagnosis. The President is Dr. Joseph F. Dorsey of Boston.

TUMORS OF THE GASSERIAN GANGLION

TUMOR OF THE LEFT GASSERIAN GANGLION ASSOCIATED WITH ENLARGEMENT OF THE MANDIBULAR NERVE

A REVIEW OF THE LITERATURE AND CASE REPORT

HENRY M. CUNEO, M.D., AND CARL W. RAND, M.D.

Department of Neurosurgery, University of Southern California School of Medicine, Los Angeles, California

(Received for publication March 7, 1952)

THE trigeminal nerve and its ganglion may be the site of a variety of pathologic lesions. Primary tumors may arise either in the Gasserian ganglion itself or in the root of the trigeminal nerve. Meningiomas, neurofibromas, gliomas, ganglioneuromas, adamantinomas, gummas, and metastatic carcinomas are some of the various tumors that have been described. In addition, sarcomas and osteochondromas of the mandible, antrum, nasopharynx or internal ear, have been reported. Aneurysms of the internal carotid artery may also cause symptoms similar to those of tumors. The clinical findings and symptoms that these lesions may produce may make localization of the lesion, whether in the ganglion itself or in the nerve root, relatively simple. On the other hand, it may be impossible at times to determine preoperatively whether the tumor is in the middle or the posterior fossa of the skull, or both.

Sachs,[13] in 1917, writing of tumors of the Gasserian ganglion, mentioned that the earliest case was reported by Dixon in 1846, and one was reported by Günsburg in 1849. Peet,[12] in 1927, found a total of 63 cases in the literature, and referred to a case studied as early as 1836 by R. W. Smith and reported in 1849. Peet described 2 cases of his own in which the tumors had infiltrated the Gasserian ganglion by direct extension through the maxillary division. In his first case the diagnosis was medullary squamous cell carcinoma, without cornification. In the second case, the maxillary division had been infiltrated extracranially by a squamous cell carcinoma of the right antrum. Microscopic examination of the sensory root and posterior portion of the ganglion showed no pathologic change.

Learmonth and Kernohan,[10] in 1930, described a tumor of the Gasserian ganglion said to be similar to neurocytoma of the retina, or similar to schwannomas of the peripheral nerves. Complete removal was not possible. Gradual anesthesia of the entire 5th nerve distribution on the left developed. Preceding each advance of anesthesia, severe transitory pain was present, and paralysis of the left face developed. In the 10 months previous to surgery, 30 corneal ulcers of the left eye had occurred.

Bradley,[2] in 1931, reported a neurocytoma of the Gasserian ganglion, the size of a cherry. The roots entering the ganglion were of normal size.

Cooper,[5] in 1933, reported 3 cases of tumor of the Gasserian ganglion—a schwannoma or sheath neuroma, a neurocytoma, and a fibroblastoma.

The schwannoma was a discrete tumor eroding the petrous portion of the temporal bone. It measured 2×1.5×0.5 cm. Following surgery, there was some defect in hearing on the left, residual pain in the left cheek and mouth, and palsy of the left 7th nerve. Seven weeks after operation there was complete left 5th, 7th, 9th, 10th and 12th nerve palsy, and bilateral involvement of the 8th nerve, more on the left side. The posterior fossa was explored by Dr. F. C. Grant and a tumor, 1 cm.×5 mm.×7 mm. in size and situated directly over the foramen lacerum posterius, was removed. It had the same microscopical structure as the tumor removed from the middle fossa.

Cooper[5] commented that clinical diagnosis is not always possible. Occasionally tic douloureux, atypical neuralgia, postzoster neuralgia, lues, tuberculosis, or an angle tumor may produce a clinical picture that cannot be distinguished from that of early tumor of the Gasserian ganglion. Exploration is justifiable in patients who suffer constant trigeminal pain not satisfactorily explained, and also in patients with objective indications of interruption of the trigeminal motor or sensory pathways without evidence of etiology other than ganglion tumor. Palliative section of the sensory root is justifiable when extirpation of the tumor is not feasible.

In 1932, Dandy[7] found 18 tumors during 250 cerebellar explorations for trigeminal neuralgia. Unfortunately, he did not classify them. He stated that gross lesions, such as free arterial loops which lifted the sensory root from the brain stem, or venous branches crossing the nerve, were responsible for the trigeminal neuralgic pains in one-third of the cases.

Cohen,[4] in 1933, tabulated all reported primary and secondary tumors of the Gasserian ganglion. Of 81 tumors, 22 were primary and 59 secondary. Thirty-three (and 1 questionable one) were exposed at surgery.

In 1935, Chang[3] reported the successful removal of a neurofibroma of the Gasserian ganglion. Krayenbühl,[9] in 1936, reported 2 cases, both neurofibromas. In one the patient died following a spinal puncture. Autopsy showed that the tumor arose in the sheath of the 5th nerve behind the ganglion, the bulk of the tumor being in the cerebellopontine angle on the left. The rostral part of the tumor arose in the Gasserian ganglion. He commented that the clinical features closely fitted those of an acoustic neurinoma. His second patient had a 6-year history of headache, sensory disturbance in the right side of the face, staggering, deafness, and mental deterioration. Ventriculography showed bilateral, symmetrical, internal hydrocephalus. No operation was performed. The patient died 2 years later. Autopsy revealed a tumor, 7×4×2.5 cm., in the right cerebellopontine angle; it extended into Meckel's cave and beneath the floor of the 3rd ventricle. At the junction of the pons, the right 5th nerve was separated into two parts by the tumor. At its origin, the nerve was distinct from the tumor but in the distal part it was spread out diffusely and incorporated in the capsule of the tumor.

Krayenbühl,[9] reviewed 54 cases of primary tumor of the Gasserian

ganglion, or root. In only 29 cases could the exact origin of the tumor be determined. In 26 cases, the tumor arose from the ganglion. He stated that the order in which symptoms appeared in these 54 cases made it possible to judge in every case whether the tumor originated in the middle or in the posterior fossa. He concluded that pain occurs when the ganglion is primarily involved and is usually absent when the tumor begins on the root. He also referred to the difficulty in distinguishing between tumor of the 5th cranial nerve root and an 8th nerve tumor. With tumor of the 8th nerve, the degree of deafness and vestibular loss is usually greater than the degree of 5th nerve sensory loss on the side of the lesion. With tumors involving the 5th nerve root, the degree of objective sensory loss is not always greater than the degree of deafness, so that precise differential diagnosis cannot be made. Their almost invariable forward extension into the middle fossa often produces ocular palsies. The presence of ocular palsies is a not uncommon finding with aneurysms of the internal carotid artery.

Cushing and Eisenhardt,[6] in 1938, divided the Gasserian tumors into three principal groups: meningiomas, neurinomas, and tumors of malignant type.

In 1939, Fitzwilliams and Fell[8] reported a case of metastasis in the Gasserian ganglion 1½ years following radical breast surgery with subsequent implantation of radium needles. The tumor was of the scirrhous type. Autopsy revealed a basal meningitis with fluid pus on the meningeal surface. The brain was adherent near the right internal auditory meatus. No growths were found in the brain. A secondary carcinoma was present in the right Gasserian ganglion, the source of the meningitis.

Love and Woltman,[11] in 1942, reported 2 cases with classical histories and signs of tic douloureux in which tumor of the ganglion was an incidental finding—a meningioma, and an epidermoid tumor. They mentioned a case of Adson's in which a meningioma of the right Gasserian ganglion was found during an operation for what was thought to be true tic douloureux. They stated that with tumors of the Gasserian ganglion pain is usually constant and often intense. It is not affected by eating, talking, shaving, or other external stimuli, as in tic douloureux. As a rule, paresthesia and sensory changes occur early. Shelden, according to Love and Woltman, pointed out that sensory changes may be lacking entirely, even when the ganglion has been almost completely destroyed, and that there may be disassociation of pain and temperature. This latter is also characteristic of involvement of the root of the 5th nerve. Usually paralysis of the motor root will be evident, following which the nerves in the region of the ganglion, especially the 4th cranial, will show involvement. The pain, so typical of tic douloureux, sometimes (but rarely) occurs with tumors of the 8th nerve, tumor of the pons, or multiple sclerosis. In the latter condition, the pain is often bilateral because of the central location of the lesion, and it may be relieved by section of the sensory root of the 5th nerve.

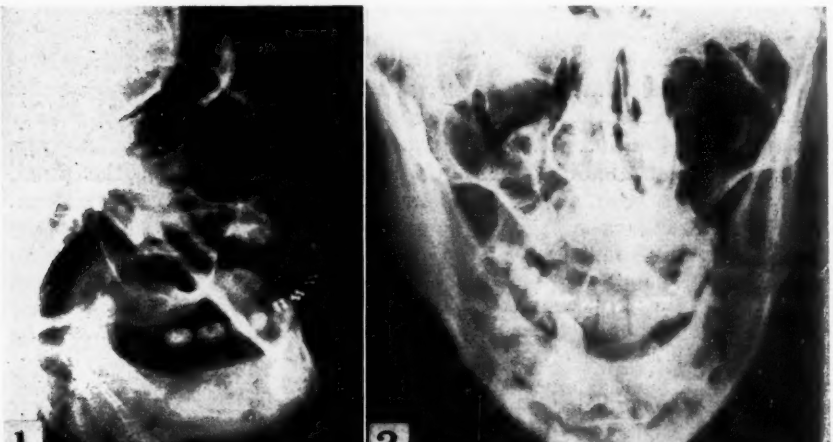
Alexander,[1] in 1947, reported a case of central neurofibromatosis in

which *nodular* tumors involved both 5th nerves, the 6th and 8th on the right while *diffuse* tumors of the right 3rd and 7th nerves were found. These were all neurofibromas. No cutaneous pigmented areas were present. He mentioned that polyneuritis cranialis must be considered with such diffuse intracranial involvement. This form of polyneuritis involves chiefly the 5th to the 12th cranial nerves in various combinations, and results from local disease—infections, toxic, degenerative or neoplastic. It may accompany polyneuritis of the limbs.

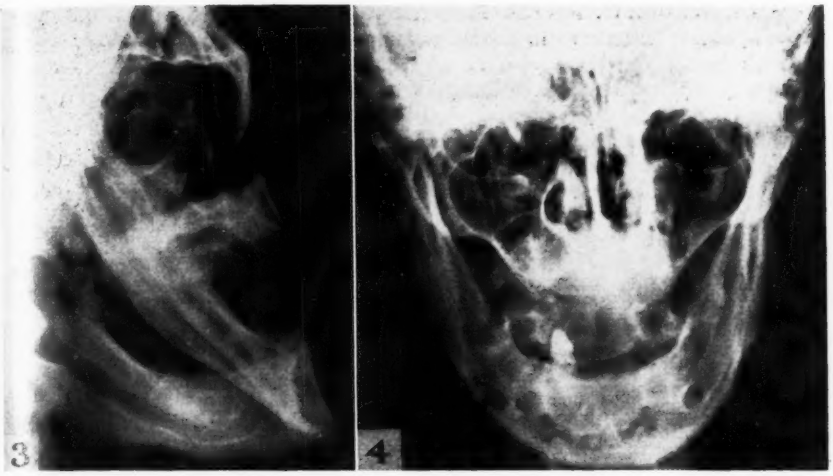
CASE REPORT

TUMOR OF THE LEFT GASSERIAN GANGLION ASSOCIATED WITH MARKED ENLARGEMENT OF THE MANDIBULAR NERVE

J.W.S., a 37-year-old white male, was first seen on Mar. 13, 1951. Two years previously he had first noted a burning numbness in his left lower lip and chin, which gradually became more painful. The numbness continued, but the pain eased up for about a year. What pain he had was confined to the left lower lip and the distribution of the mental branch of the mandibular nerve. About September 1950, he began having pain in the left lower jaw. Four months later pain started in the tragus of his left ear and spread over his left cheek. There was soreness behind the left ear in the stylomastoid region. He also described pain on the anterior two-thirds of the left side of his tongue—a "kind of burning, like cigarette or tobacco bite." For the last 6 weeks he had had no freedom from discomfort in the left side of his face. He had also had some shooting pain from the left stylomastoid region to the angle of the left lower jaw. The pain did not go down the jaw, but at times he had pain in the region of his left lower lip and chin. Eating did not necessarily bring on the pain, although if he had pain, eating was troublesome. Shaving the



FIGS. 1 and 2. Roentgenograms, Oct. 21, 1949. (1) Lower jaw, showing the dental canal of normal size on the left side. (2) Showing both mental foramina of equal size.



FIGS. 3 and 4. Roentgenograms, Jan. 3, 1951. (3) Showing extraordinary enlargement of the inferior dental canal on the left side. (4) Showing enlargement of the left mental foramen.

left side of his face was always painful. He thought there was some numbness of the left side of his face, compared to the right. He had had no pain in the left eye, left side of his nose or forehead, and his left nostril had been free of pain at all times. He had had no discomfort in the right side of his face.

Examination. The cranial nerves were entirely normal, with the exception of the left 5th. There was slight numbness of the left lower lip in the region supplied by the mental branch of the mandibular nerve. There seemed to be slight numbness of the tragus of the left ear, compared to the right. Otherwise, one could not outline any definite objective sensory changes. The corneal reflexes were active and equal and there was no anesthesia of the cornea. The motor component of both 5th nerves was intact and no evidence of wasting of the muscles of mastication was present. Both 7th nerves were normal. There were no other neurologic abnormalities.

Roentgenograms (lower jaw). *Oct. 21, 1949* (Fig. 1): "The dental canal is of equal size on both sides of the mandible. The mental foramina (Fig. 2) are normal and equal in size." *Jan. 3, 1951* (Fig. 3): "There is extraordinary enlargement of the inferior dental canal and mental foramen (Fig. 4) on the left side. This enlargement apparently took place between Oct. 21, 1949 and Jan. 3, 1951. Enlargement of the mandibular nerve seems likely. The possibility of a tumor in this case must be considered, although its exact nature is not clear." *Mar. 26, 1951:* "There is enlargement of the mandibular foramen on the left and the mental foramen on the left, and the canal within the bone which unites them is enlarged, as was shown on films of Jan. 3, 1951. The enlarged canal within the bone ends abruptly at the mental foramen and does not continue toward the symphysis. The vertical stereo shows a foramen ovale of normal dimensions on the right. On the left (Fig. 5) it is enlarged into a circular foramen of the same dimensions as the canal within the left mandible."

Impression. All evidence pointed toward enlargement of the left mandibular

nerve, beginning as high as the Gasserian ganglion and extending throughout the entire length of the nerve to the mental foramen. This suggested von Recklinghausen's disease, but there were no other clinical manifestations of the disease.

Course. Exploration of the ganglion seemed justifiable. On April 17, 1951, biopsy of the mental nerve was reported as showing "marked inflammatory change and fibrosis in peripheral nerve (left mental)—etiology not apparent."

Reexamination, Aug. 16, 1951. The patient was not having so much pain but had noticed discomfort and numbness creeping up the left side of his face and cheek. He also thought there had been a little swelling along the lower jaw inside his mouth. His face was definitely swollen on the left. He had hypesthesia to pin-prick and touch in the distribution of the left mandibular division, and moderate hypesthesia in the distribution of the maxillary division, but no involvement of the ophthalmic division.

FIG. 5. Roentgenogram, Jan. 3, 1951. Showing enlargement of the left foramen ovale.

Roentgenograms, Aug. 17, 1951. The foramen ovale on the left side had increased slightly in size since Mar. 26, 1951. It was approximately three times the average size. The large mandibular canal on the left was again demonstrated. There was no definite change in the appearance of the mandible since the previous films.

Operation, Sept. 4, 1951. The usual approach to the Gasserian ganglion through the temporal route was made. After the middle meningeal artery was coagulated and cut, the dura was further dissected medially and a large reddish-gray tumor, 1.5 cm. in diameter, was encountered. It was globular in shape and comprised the enlarged Gasserian ganglion. Dissection was continued posteriorly until the tumor was completely mobilized and free. The sensory root of the 5th nerve was sectioned posterior to the ganglion. The motor root was not identified. The tumor was teased forward, freeing it from the wall of the cavernous sinus. The tumor extended into the 2nd and 3rd divisions, but did not seem to invade the 1st division grossly. All three divisions were cut and the tumor was then removed in three pieces. The foramen ovale was about three times the normal size. The tumor tissue that extended into the foramen rotundum and ovale was cauterized. The distal portion of the ophthalmic division, which appeared grossly normal, was not cauterized for fear of damage to the nearby oculomotor and trochlear nerves.

Pathologic Report (Dr. L. J. Tragerman). "There is a large coarse nodular structure suggesting possible pre-existing bundles of fibres. These nodules are occupied by cells of two principal appearances. One is in the form of solid masses, with a tendency to gland-like arrangement, but without glandular formation. The individual cells are characterized by distinct cell borders, pale to coarsely granular cytoplasm and large pale nuclei. Nucleoli are prominent. The other cell-type pattern is that of a spindle-cell proliferation. One sees the preponderance of large pale cells

resembling epithelial cells. In some areas the cells are spindle in type, with elongated oval nuclei. The tumor appears histologically malignant. Diagnosis: Probable malignant schwannoma."

Pathologic Report (Dr. Cyril B. Courville). "Nine slides were studied which were stained with hematoxylin and eosin, phosphotungstic acid hematoxylin, and Perdrau stains. This appears to be a tumor which is pressing into the nerve. The architecture is most unusual but suggestive of a neurofibroma."

Final Diagnosis. Unclassified tumor which resembles a neurofibroma (Fig. 6).

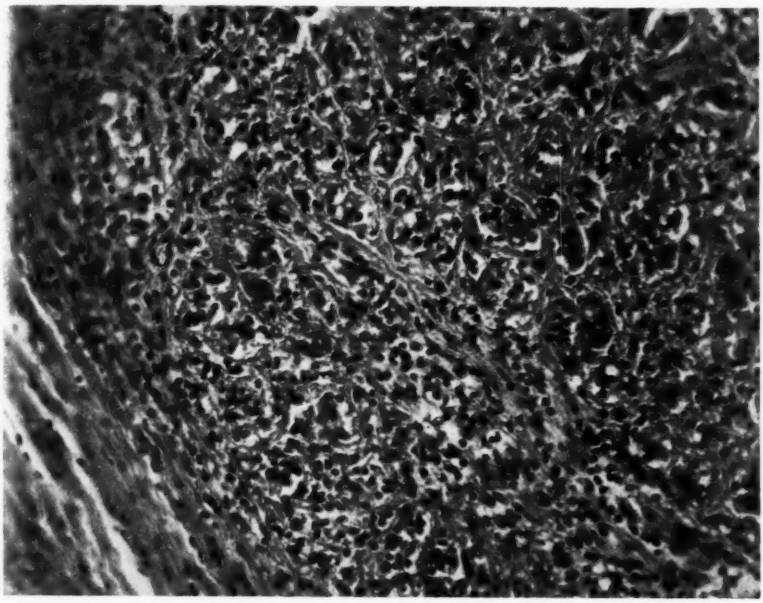


FIG. 6. Photomicrograph of tumor of the Gasserian ganglion showing the unusual architecture suggesting probable malignant schwannoma or neurofibroma.

Reexamination, Dec. 31, 1951. The patient had noted intermittent swelling in the region of the left temple. At times he had had twinges of pain above the left zygoma, upper eyelid, and in the low frontal region. He had some very slight discomfort most of the time, and occasionally sharp transitory pain. There was anesthesia in the entire left trigeminal distribution. It was less marked in the 1st division, and corneal sensation was retained. There was slight motor weakness of the left 5th nerve, the jaw deviating to the left.

COMMENT

Tumors of the Gasserian ganglion may be either primary or secondary. In 1933, Cohen[4] reported a total of 81 tumors of the ganglion, of which only 22 were primary, and 59 were secondary. Apparently endothelioma is the most common type of primary tumor, followed by fibrosarcoma, and neurofibroma, other types being extremely rare.

It is possible in some cases to determine the origin of the tumor (whether in the middle or posterior fossa) when the trigeminal nerve is involved. The order in which symptoms appear is of great importance. Pain occurs when the Gasserian ganglion is primarily involved and is usually absent when the tumor begins on the sensory root. The onset of pain in the distribution of the 5th nerve, which later decreases or disappears, should make one suspect extension of the tumor from the ganglion along the sensory root into the posterior fossa. Lower cranial nerve palsies, cerebellar or cerebral peduncle signs should point to involvement of the posterior fossa by the tumor. It may be very difficult to distinguish between tumor of the 8th nerve (acoustic neurinoma) and tumor of the 5th cranial nerve root. The degree of deafness with 8th nerve tumor and vestibular loss is greater than the degree of 5th nerve sensory loss on the side of the lesion. In tumors involving the 5th nerve root, the degree of objective sensory loss is not always greater than the degree of deafness, so that precise differential diagnosis cannot be made. Sensory changes may be lacking entirely, even when the ganglion has been almost completely destroyed. There may be disassociation of pain and temperature, this latter being also characteristic of involvement of the 5th nerve root. Usually paralysis of the motor root can be demonstrated, and at times involvement of the 3rd and 4th cranial nerves, which are in close proximity to the ganglion, will appear in the presence of a tumor of the ganglion. The pain, so typical of tic douloureux, may on rare occasions occur with tumors of the 8th nerve, tumor of the pons, atypical neuralgia, postzoster neuralgia, lues, tuberculosis, and multiple sclerosis. In the latter case the pain is often bilateral.

It was indeed fortunate that roentgenograms of the mandible were made at the onset of this patient's symptoms, which could be compared with subsequent views. These show the rapidity with which this tumor had invaded the entire mandibular canal, including the mental foramen, between Oct. 21, 1949 and Jan. 3, 1951. One cannot help but wonder if similar lesions may have sometimes escaped detection and been classified as atypical neuralgia, because of the few objective clinical findings, and the peculiar nature of the subjective complaints.

CONCLUSION

An unusual case of tumor involving the Gasserian ganglion and the mandibular and maxillary divisions of the trigeminal nerve is reported. One can only speculate as to whether the tumor arose primarily in the ganglion and subsequently spread along the entire mandibular division, later involving the maxillary division, or arose primarily in the mandibular division, and later involved the Gasserian ganglion. The diagnosis of probable malignant schwannoma was made by one pathologist, that of an unclassified tumor resembling a neurofibroma by another. From the appearance of the enlarged mandibular canal, without further invasion of the mandible, it would appear that this was a rapidly growing primary tumor

of the mandibular nerve, a malignant schwannoma, which involved the Gasserian ganglion.

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LOCALIZATION OF INTRACRANIAL LESIONS BY RADIOACTIVE ISOTOPES*

WILLIAM T. PEYTON, M.D., GEORGE E. MOORE, M.D., LYLE A. FRENCH, M.D., AND SHELLEY N. CHOU, M.D.

Divisions of Neurosurgery and General Surgery, The Medical School, University of Minnesota, Minneapolis, Minnesota

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IN OCTOBER, 1946 Moore[3] injected sodium fluorescein into patients with gastric carcinoma with the thought that when the tumor was exposed at laparotomy and viewed under ultraviolet light, it might accentuate the difference between normal and carcinomatous tissue. Early in 1947 the same procedure was carried out with patients operated upon for brain tumor. It was found to be much more differential in brain tumors; almost invariably the tumor fluoresced. The technique established for best differential fluorescence was to inject 5 cc. of 20 per cent sodium fluorescein solution an hour or more before the tumor was exposed.

Cortical or dural tumors can be fluoresced directly with a C.H. 4 Mercury Vapor lamp equipped with a Wood's filter. In case of subcortical tumors, needle biopsies are taken through small openings in the exposed dura and examined. This method has been very helpful in distinguishing abnormal tissue.

Radioactive diiodofluorescein (DIF*) was synthesized at this clinic[1] and later a more pure product was developed by Tabern.[6] After radioactive diiodofluorescein was injected intravenously, gamma activity over the head was measured with a single shielded window type Geiger-Müller counter. The first such count was made in September, 1947. Since that time, up to July 1, 1951, counts have been made in approximately 330 patients.

Not more than 1.9 μc., but as a rule, more than 1.0 μc. of I^{131} is injected and counting is started 30 minutes or more after injection of the diiodofluorescein. Counting rates were determined at various areas over the head and comparison was made between symmetrical areas on the two sides of the head for localization of tumor. The symmetrical areas on each side are measured one after another because the general level slowly drops.

More recently radioactive iodinated human serum albumen RIHSA* has been used instead of DIF*.[2] The amount of RIHSA* injected intravenously is 5 μc. per kg. of body weight. It remains in the blood stream for a longer time than DIF*, making the radioactivity stable while the original survey is made, and recheck of suspicious areas can be compared directly with the original counts or a second survey can be made 24 or even 48 hours later without injecting more radioactive solution.

We have tried various types of Geiger-Müller counters and also a scinti-

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lation counter which gives very much higher counts; hence, the same percentage differences should be much more significant. At the present time, we are about to try a multiple counter consisting of a bank of 18 tubes arranged so that they will survey both sides of the head simultaneously. Since we have only 8 scalers, they are used in groups of 8 at a time.

Some of our earlier experiences in localizing brain tumors by this method have been reported.[5] In the first 26 cases, 10 tumors were correctly localized and 8 were not; 2 vascular lesions were correctly localized and in the other 6 cases, tumors were correctly excluded. Therefore, of 16 tumors, 62 per cent were correctly localized.

Later, 77 cases were analyzed.[4] Forty-nine of them were tumors, of which 25 or 51 per cent were correctly localized and 24 or 49 per cent were not. In the remaining 28 cases a correct diagnosis was made in 25, in most of which there was no focal lesion, but a few vascular or demyelinizing lesions were correctly localized. One brain abscess was not localized. In these 77 cases the radioactive isotope diagnosis of a localized lesion or absence of a focal lesion was correct in 65 per cent.

Since we began to use a new type of Geiger-Müller tube made by the Texas Company and furnished to us by them, the results have improved. This Texas tube was used from September 15, 1950, to April 1, 1951; and, during this period, 71 patients were tested. The results obtained in these 71 cases are given in Table 1.

TABLE 1

Radioactive counting for intracranial diagnosis Sept. 15, 1950 to April 1, 1951

71 cases	
14 excluded—no final conclusive diagnosis	
57 cases—diagnosis correct in 43 or 75%	
26 brain tumors	
17 (65%) correctly localized	
9 (35%) incorrectly diagnosed	
31 non-tumor cases	
26 (81%) no focus or correct focus for lesion present	
5 (18%) incorrect diagnosis	

Fourteen cases are excluded because to date it has not been established whether the isotope localization diagnosis was correct or not. In the remaining 57 cases, there were 26 brain tumors; 17 were correctly localized and 9 were not. Hence the localization was correct in 65 per cent of the patients having tumors. Thirty-one did not have tumors. Some of these did have vascular or demyelinizing lesions which gave a localizing high count over the lesion. In these 31 cases, the radioactive isotope diagnosis of a localized lesion or the absence of a focal lesion was correct in 26 and wrong in 5. Thus the diagnosis was correct in 81 per cent of this group. In the entire 57 cases, either absence of a focal lesion was properly demonstrated or a correct localization of a focal lesion was made in 43 or 75 per cent.

We tried to be as objective as possible in making the diagnosis by the isotope study in the above groups. The patients' clinical records were not utilized. Sometimes the examiner was influenced by physical signs that were very obvious, such as aphasia or hemiplegia. To test this factor and also see how consistent the interpretation of these records would be on a second evaluation, the same 71 records compiled since September 15, 1950, were again examined and interpreted by the same person who had made the original interpretation. In this second survey, all data on the record that might identify it or give a clue to the previous interpretation were effaced. The second interpretation varied from the first in 8 of the 71 records. Five of these were previously correct and now wrong. The other 3 were in the 14 with still unsettled diagnoses.

It is clear that there are limitations to the accuracy of this method. Any localized lesion that destroys the blood-brain barrier will give a positive focus. In the cases here surveyed a focus of increased activity was found in association with a chronic subdural hematoma, and in a patient with psychomotor seizures a focus was found over the temporal lobe which on removal was found to contain a focal area of demyelinization. It is possible that encephalitis, at least in the more acute fulminating form, may so affect the blood-brain barrier as to produce a focus of high counts. Vascular lesions will at least sometimes give a positive focus. A case of thrombosis of the internal carotid artery in which there was a definitely positive focus over the left frontal region was in the group under analysis. In this case we were led on by the isotope localization to make the correct diagnosis after a negative ventriculogram.

CASE REPORTS

Case 1. A 55-year-old farmer had noticed clumsiness in his right lower extremity for 4 years. There was some recent progression. In the 2 months preceding hospitalization, numbness in the right lumbar region and right thigh was observed. There was also some difficulty in writing and speaking.

It was obvious that his mentation was slowed. There was paresis of the right lower extremity and to a lesser extent in the right arm. The reflexes were hyperactive on the right and the Babinski reflex was extensor on the right.

A left carotid angiogram was done but only the external carotid artery filled. A ventriculogram was normal. With these findings and yet a very positive focus by radioactive isotope count (Fig. 1) we were led to make a diagnosis of internal carotid artery thrombosis. This diagnosis was verified first by repeating the angiogram; again only the external carotid artery filled. A segment of the thrombosed left internal carotid artery was then excised.

Case 2. A 51-year-old woman had had a right-sided acoustic neuroma completely removed here in 1944. Thereafter, she did her housework and was quite well until 1947 when she began to complain of loss of hearing in the other ear. This progressed and she was admitted to the hospital in September 1950, with a complete loss of hearing and inability to walk.

There was no response from either labyrinth. The reflexes were hyperactive on

the right side. It was thought that she now had a second acoustic neuroma, this time on the left side. She was about to be operated upon for such a lesion when the radioactive isotope count was made and showed a focus in the left frontoparietal region (Fig. 2). On repeated test this focus persisted. Because of these counts it was assumed that she probably had a meningioma associated with multiple neurofibromatosis. Ventriculography confirmed the presence of a left cerebral lesion and operation revealed multiple meningiomas over the left hemisphere; the largest was located parasagittally in the parietal area. Here, the radioactive isotope count led to the correct diagnosis.

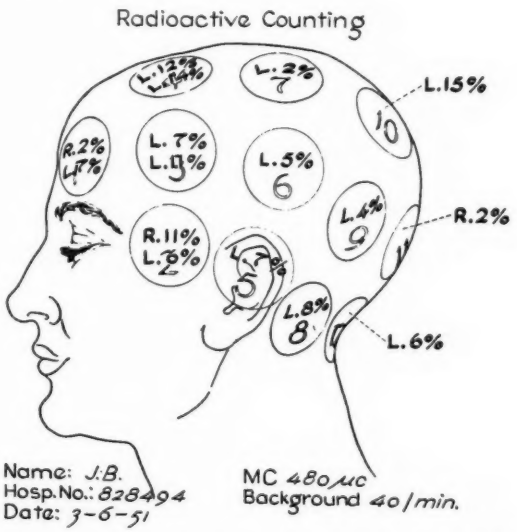


FIG. 1. *Case 1.* Thrombosis of left internal carotid artery. High counts in left frontal region. Light figures are the positions counted. Heavy percentage figures signify the percentage by which the counts were higher on the right (R) or the left (L) side. In positions 1, 2, 3, and 4 counts were repeated; hence, two percentage figures at each of these locations with reversal of the side of high count in positions 1 and 2.

It would appear that in the present state of development of radioactive isotope localization, the clinical history and findings must at least sometimes be considered in making a diagnosis; but if isotope encephalometry reveals a good focus which is consistently present on recheck, it is most probable that this is the site of the lesion. Glioblastomas, metastatic tumors and meningiomas, parasagittal or elsewhere over the vault, usually give a very definite focus. If there is a less evident focus or no focus, then the radioactive isotope count should be reviewed in conjunction with the clinical history and findings. Recounts should be made frequently at this time. This can readily be done if radioactive iodinated human serum albumen is used as the tracer agent.[4] When this agent is used the differential uptake between tumor and normal brain tissue remains for 48 hours or more. It may be possible to cor-

relate the radioactive count and clinical findings even though considered independently they seem to disagree, or a focus with insufficient differential to be diagnostic when considered alone may be considered significant when it agrees with the clinical diagnosis. To illustrate, 2 cases from the group are reported. In Case 3, a patient with a glioblastoma, a very definite focus was

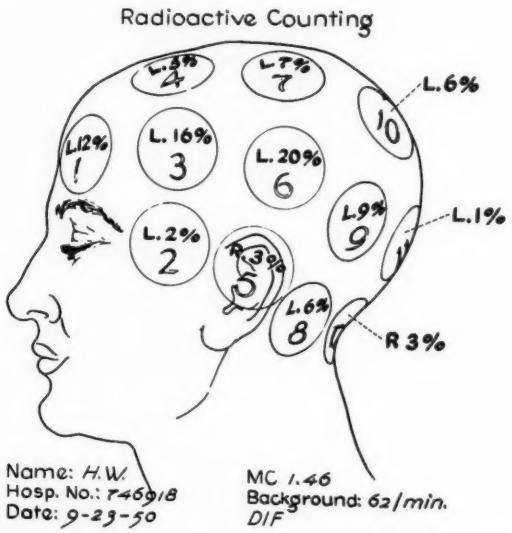


FIG. 2. *Case 2.* Multiple meningiomas over left cerebral hemisphere. High counts over left frontoparietal region. *DIF* signifies that diiodofluorescein was injected. Designations otherwise as in Fig. 1.

found which persisted on recheck. In Case 4, the radioactive isotope count in conjunction with clinical data was diagnostic.

Case 3. A 68-year-old man gave a history of progressive mental confusion for the past month. Hyper-reflexia on the right suggested a lesion of the left hemisphere. A very definite left fronal lobe focus was found with high counts over most of the left side, indicating cerebral edema of this hemisphere (Fig. 3). This focus persisted when rechecked. With such findings, one can be quite certain that localization is correct. The patient had a large left frontal glioblastoma removed at operation.

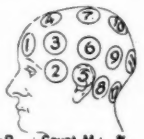
Case 4. A 54-year-old woman, 9 months before admission to the hospital, had a sudden onset of very severe headache of 1 week's duration. Since that time she had intermittently less severe headaches. There was a progressive lethargy. Except for the lethargy there were no neurological abnormalities. A 3rd ventricle tumor was suspected. The counting was interpreted as demonstrating no focus, but after a 3rd ventricle tumor was demonstrated by ventriculography, it was obvious on review of the radioactive counts that there really was a localized high count bilaterally equal at position 5, in which the counting tube is directed at the 3rd ventricle (Fig. 4).

In Case 4, which we have recorded here as an example of incorrect localization, the lesion should have been correctly localized if a less objective procedure had been followed.

There are biological limitations to this method; necrotic tissue or cysts

Radioactive Counting

Hosp. No.: 796947 Name: E. B.
Date: 10-8-50 Age: 68 yrs.
MC 1.56
Background: 50/min.
DIF*



Position	Count/m-B	Count M	%	Count/m-B	Count M	%
R1	1602-50	1552	L			
L1	1726-50	1676	T			
R2	1666-50	1616	L	1622-50	1572	L
L2	2011-50	1961	18	1684-50	1634	4
R2				1640-50	1590	L
L2				1900-50	1850	14
R3	1582-50	1532	L	1430-50	1380	L
L3	1952-50	1902	19	1784-50	1734	20
R4	1677-50	1627	L			
L4	1897-50	1847	12			
R5	1579-50	1529	L			
L5	1633-50	1583	3			
R6	1413-50	1363	L			
L6	1511-50	1461	T			
R7	1656-50	1606	R			
L7	1621-50	1571	2			
R8	1540-50	1490	R			
L8	1533-50	1483	0			
R9	1450-50	1400	L			
L9	1560-50	1510	T			
R10	1651-50	1601	L			
L10	1663-50	1613	0			
R11	1584-50	1534	R			
L11	1504-50	1454	5			
R12	1444-50	1394	L			
L12	1513-50	1563	4			

FIG. 3. *Case 3.* Left frontal glioblastoma. Figures in circles represent the positions counted on each side. Very high counts in positions 2, 3, and 4 in heavy type. They persisted on repeated counts at positions 2 and 3 (last three columns).

do not take up the radioactive material and the site of the lesion may therefore give even a lower than normal count. This is illustrated by Cases 5 and 6.

Case 5. A 60-year-old man complained of loss of vision, headache and vertigo of 4 months' duration. There was severe papilledema with retinal hemorrhages. Tendon reflexes were hyperactive on the right, but the pineal gland was displaced to the left.

High radioisotope counts were obtained bilaterally over the frontal areas, with higher counts on the left, but the difference was in no instance greater than 9 per cent (Fig. 5). After angiography and ventriculography both demonstrated this

tumor to be in the right frontal lobe, operation was performed and a glioblastoma of the right frontal lobe extending across the midline into the medial part of the left frontal lobe was removed.

In view of the operative findings in Case 5 it is not surprising that the

Radioactive Counting

Hosp. No.: 830196 Name: M. L.
Date: 3-11-51 Age: 54 yrs.
MC 0.6 + 200 μc.
Background: 60/min.
DIF* and RIHSA

Position	Count/m-B	Count M	%	Count/m-B	Count M	%
R1	851-60	791	R			
L1	822-60	762	4			
R2	1300-60	1240	L			
L2	1323-60	1263	1			
R3	1073-60	1013	L			
L3	1074-60	1014	0			
R4	1115-60	1055	R	1006-60	1000	R
L4	1010-60	950	10	983-60	923	8
R5	1339-60	1279	R			
L5	1384-60	1324	3			
R6	952-60	892	R			
L6	907-60	847	6			
R7	1023-60	963	R			
L7	967-60	907	6			
R8	1298-60	1238	R	1326-60	1260	R
L8	1168-60	1108	11	1319-60	1259	0
R9	925-60	865	R			
L9	923-60	863	0			
R10	954-60	894	L			
L10	974-60	914	2			
R11	1208-60	1148	R			
L11	1201-60	1141	0			
R12	1400-60	1340	L			
L12	1320-60	1260	6			

FIG. 4. *Case 4.* Tumor of posterior part of 3rd ventricle. See legend to Fig. 3. High counts at position 5 on each side. *DIF** and *RIHSA* indicate that both diiodofluorescein (DIF) and radioactive iodinated human serum albumen (RIHSA) were used.

counts were highest on the left side. That part of the tumor that was in the right frontal lobe was largely necrotic and cystic while the portion extending across the midline into the left frontal lobe was solid tumor which took up dye much better.

Case 6. A child, 23 months old, was admitted to the hospital because he had had seizures since the age of 4 months. His development was retarded. It was thought

he had a left cerebral lesion as evidenced by the type of seizure, clumsiness of the right arm and hyperactive tendon reflexes on the right.

The radioactive isotope count showed what appeared to be a good focus in the right frontal region because the counts on the right side were so much higher than on the left. But, transillumination showed the anterior part of the left frontal

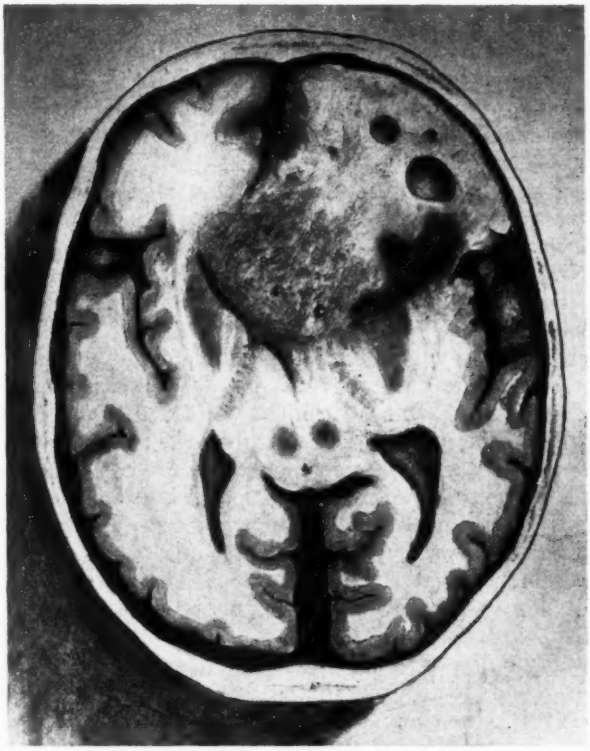


FIG. 5. *Case 5.* Cystic glioblastoma of right frontal lobe with the more solid portion extending across the midline.

region to be cystic and operation confirmed the presence of multiple cysts replacing the anterior part of the left hemisphere.

In Case 6, a correct localization by radioactive isotope count could be made only when interpreted with relation to the clinical signs. Lower counts on the side of the lesion were due to decreased uptake of dye by the cysts.

The radioactive isotope diagnosis was incorrect in 9 cases. The reason for error in 2 of them is discussed above. Some comment should perhaps also be made concerning the reason for failure in the other 7 cases.

1. A glioma of the pons gave a fairly good, but false focus over the left

parietal region. A single recheck confirmed this focus; but, if the clinical diagnosis had been utilized, additional checks would have been made to rule out a chance variation at this site and a false localization probably avoided.

2. A carcinoma which extended from the nasal sinuses into the base of the anterior cranial fossa was so atypical that the microscopic examination revealed only granulation tissue—yet, grossly, this was a tumor.

3. An oligodendroglioma, 2 cm. in diameter, gave no focus and was found only when the temporal lobe was being removed for psychomotor epilepsy. There are two reasons for this error: The small size of the tumor and the fact that it was an oligodendroglioma, a type of tumor that has been found to have a low uptake of dye. This tumor fluoresced poorly under ultraviolet light.

4. Another left temporal oligodendroglioma gave a right parietal focus. This tumor was found and removed when the temporal lobe was removed for psychomotor seizures. It was a large tumor, in fact, there was a minor defect in this temporal horn on ventriculography; but, at operation, it was demonstrated that the tumor did not take up enough sodium fluorescein to fluoresce under ultraviolet light.

5. A glioblastoma involved the left basal ganglia, but a radioactive isotope focus was found over the posterior part of the right hemisphere. The lesion was small and deep so that it might well fail to give a focus, but here it is impossible to explain the high counts over the left side.

6. An astrocytoma of the cerebellum gave an erroneous right parietal focus. Tumors in the posterior fossa, as a rule, are not well localized by this method because of the uptake of isotope by the overlying muscles and also the greater difficulty in properly placing the counter tube.

7. A parasellar meningioma gave no focus. The factors unfavorable for localization in this case were the small size of the tumor and its deep location at the base of the skull.

After this group of cases was evaluated it was decided that the available clinical data should be utilized in the interpretation of the radioactive counts. About this same time, April 1, 1951, we began to use a scintillation counter. Between April 1 and July 1, 1951, 49 cases were counted and interpreted in this manner. The results (Table 2) were very much more nearly accurate. Again, as in the previous group of cases analyzed, a check was made to determine how much these interpretations were influenced by the clinical data. All of the data on each record to identify it or give a clue to the previous interpretation were effaced when it was again interpreted by the same person. The results of this reinterpretation are also shown in Table 2. The percentage of correct localization dropped to essentially the same as that of the previous group which were originally interpreted without knowledge of the clinical data.

It is therefore evident that if the clinical data are utilized in the interpretation of the radioactive isotope counts the diagnostic accuracy is very high, approximately 94 per cent; but, without the help of these data, it is

approximately 75 per cent accurate. The diagnosis with the aid of clinical data was most nearly accurate when a tumor was present. In this small group of 17 tumors all were correctly localized; but when reinterpreted without the aid of clinical data, tumor localization was only 71 per cent correct or essentially the same as in the preceding group.

Since we began to utilize this method in 1947, the counting and interpretation of counts has in successive periods been done by six different observers without significant change in accuracy. During this same period progressive improvement has been made in instrumentation, but without

TABLE 2

*Isotope encephalometry in 46 cases interpreted with and without clinical data**

	Interpretation with Clinical Data		Interpretation without Clinical Data	
	No.	Per cent	No.	Per cent
Tumors correctly localized	17	100.0	12	70.6
Tumors not correctly localized	0	00.0	5	29.4
No tumor and isotope localization correct	26	89.7	24	82.8
No tumor and isotope localization incorrect	3	10.3	5	17.2
Total correct	43	93.5	36	78.3
Total incorrect	3	6.5	10	21.7

* Three of the 49 cases examined are omitted in this tabulation because the diagnosis is still undetermined.

significant improvement in accuracy, although it has facilitated making the counts. It would therefore appear that there are certain biological limitations to the method, and at least many of these are insurmountable unless clinical data are utilized in the interpretation of the radioactive isotope counts.

CONCLUSIONS

Approximately 70 per cent of intracranial tumors can be correctly localized with radioactive isotope examination alone; but, if the clinical data are utilized in the interpretation of the radioactive isotope counts, correct localization is very much enhanced, up to 94 per cent.

There are biological limitations to this method which lead to erroneous diagnoses unless the clinical data are utilized in the interpretation. Cystic and necrotic lesions do not take up the radioactive isotope and therefore may give a false localization with low counts over the lesion. Small lesions do not take up enough of the dye to give a good differential count over the lesion; and certain types of tumor, especially oligodendroglioma, appear to take up the isotope very little. Mid-line lesions (frequently they are also small) and posterior fossa lesions are difficult to localize. Lesions other than tumors but

which lower the blood-brain barrier, such as vascular lesions and possibly inflammatory and demyelinizing lesions, give a focus of high counts. Therefore this procedure does not differentiate between a neoplastic and non-neoplastic lesion.

The most easily localized lesions with isotope encephalometry are large lesions in the cerebral hemisphere associated with edema. Glioblastoma, meningioma and metastatic tumors give the best differential counts.

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SUBDURAL HEMATOMA ASSOCIATED WITH BLEEDING INTRACRANIAL ANEURYSM*

ROBERT C. BASSETT, M.D., AND LLOYD J. LEMMEN, M.D.
Department of Surgery, University of Michigan Medical School and Hospital, Ann Arbor, Michigan

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LEAKING intradural aneurysms usually produce extensive subarachnoid hemorrhage. In rare instances the bleeding may occur into the subdural space and the clinical manifestations may be those of an acute subdural hematoma.

Five such cases of subdural hematoma associated with bleeding intracranial aneurysm have been encountered within our experience with these lesions. They present additional problems in diagnosis and treatment not common to the usual aneurysm with subarachnoid hemorrhage.

CASE REPORTS

Case 1. N. P. was a 38-year-old, left-handed female who slipped on the linoleum on Mar. 17, 1942, striking her right cheek and elbow on the floor. She was confused and drowsy for 24 hours. X-rays of the skull showed no abnormality. A month later right frontal headache and vomiting developed and she became semicomatose, at which time she was referred to University Hospital.

Upon admission B.P. was 140/94; pulse rate 80, and respirations 15. She was drowsy, uncooperative and tended to perseverate. There was early bilateral papilledema. The right pupil was larger than the left. There was a mild right central facial palsy and a right hemiparesis. An extensor plantar response was present on the right.

Under local anesthesia a small bone flap was turned in the left parietal-parasagittal region. Bloody fluid and clot under increased pressure were evacuated from the subdural space. The bone flap was re-elevated 48 hours later when the patient again became comatose and totally hemiplegic. More bone was removed and a needle was inserted into the left superior temporal gyrus. Bloody fluid under increased pressure was encountered.

Angiography performed after the patient had improved showed a small aneurysm on the most proximal portion of the middle cerebral artery and elevation of the Sylvian vessels (Fig. 1).

No further treatment was instituted; she gradually improved. She has had no further difficulty for 9 years except for four grand mal seizures and occasional headache centered behind the left eye. Optic atrophy O.S. and astereognosis of the right hand persist.

Case 2. F. M. was a 45-year-old male under psychiatric treatment for chronic alcoholism and psychosis. On Aug. 23, 1945, he was struck on the occiput by a disturbed patient. He fell to the floor, arose and a few minutes later fainted and once

* Presented at the meeting of the Harvey Cushing Society, Victoria, British Columbia, June 5, 1952.

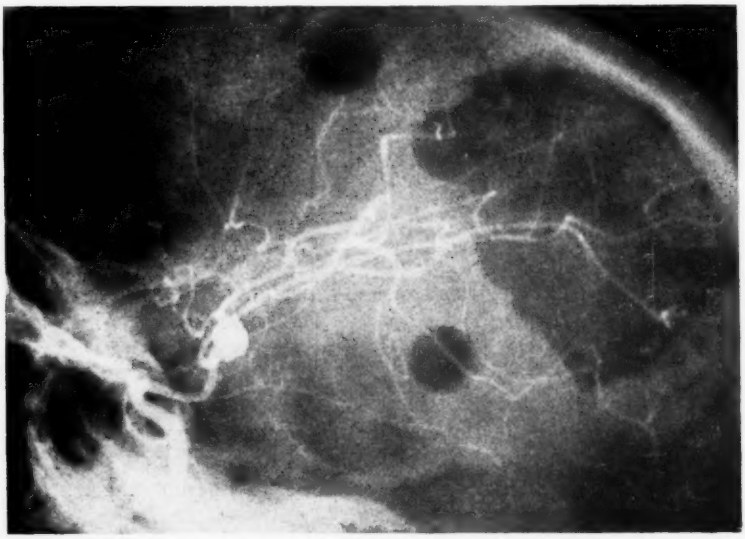

FIG. 1. *Case 1.* Aneurysm of middle cerebral artery (lateral view).

FIG. 2. *Case 2.* Aneurysm of middle cerebral artery (frontal view) with subdural clot.

again he struck his head in falling. Later that day he complained of dizziness. Two days later there developed Jacksonian fits involving the right half of his body.

The patient had an expressive aphasia. The pupils were round and equal and reacted to light. A right central facial palsy and right hemiparesis were present.

Lumbar puncture revealed a pressure of 130 mm. of water. The fluid was grossly bloody.

Angiography demonstrated a small aneurysm on a peripheral branch of the left middle cerebral artery. A subdural clot over the left hemisphere was suggested by displacement of the entire arterial system toward the right producing a $1\frac{1}{2}$ cm. space between cerebral cortical vessels and dura (Fig. 2).

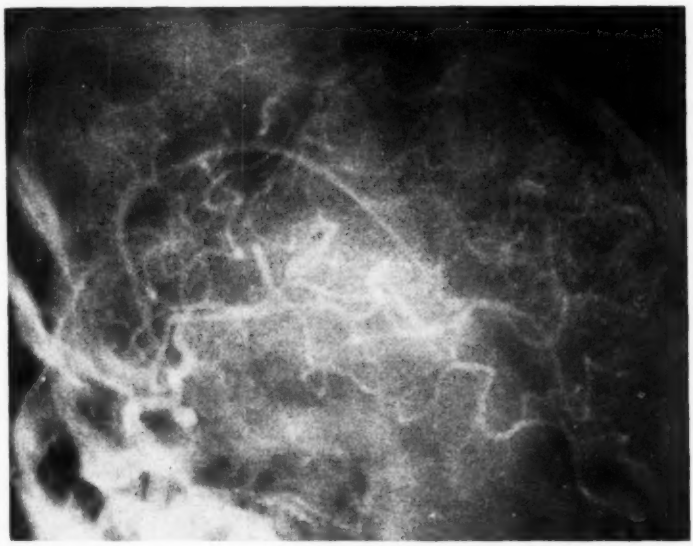

FIG. 3. *Case 3.* Aneurysm of right internal carotid artery (lateral view).

Left parietal osteoplastic craniotomy revealed a chronic subdural hematoma depressing the cortex $1\frac{1}{2}$ cm. A pea-sized aneurysm, actively bleeding, was found in the supramarginal gyrus. From this area upward toward the midline there was a triangular infarct within cortex. Inner and outer membranes of the hematoma were removed and the aneurysm was ligated and removed.

The following day the patient lapsed into deep coma. The subdural space was again explored and recurrent clot discovered and removed. The subdural space was obliterated by re-expansion of the brain by spinal infusion of Ringer's solution.

The patient made an uneventful recovery and 6 years later was adjusting well in the community. He has had convulsions which are well controlled by medication.

Case 3. H.S. was a 43-year-old, right-handed female found in a semicomatose state in the restroom of a restaurant 3 weeks before admission. She complained of pain in the right side of her head and had weakness of her left leg. Thirty minutes later she became unconscious and had a grand mal fit. Lumbar puncture revealed

grossly bloody CSF. She gradually improved, but later became more irrational and hyperactive and was referred to University Hospital on Jan. 6, 1951.

Examination revealed B.P. of 110/70, pulse rate of 76, and respirations of 20. She was disoriented and had periods of hallucination. An extensor plantar response was present on the right. There were no other localizing signs.

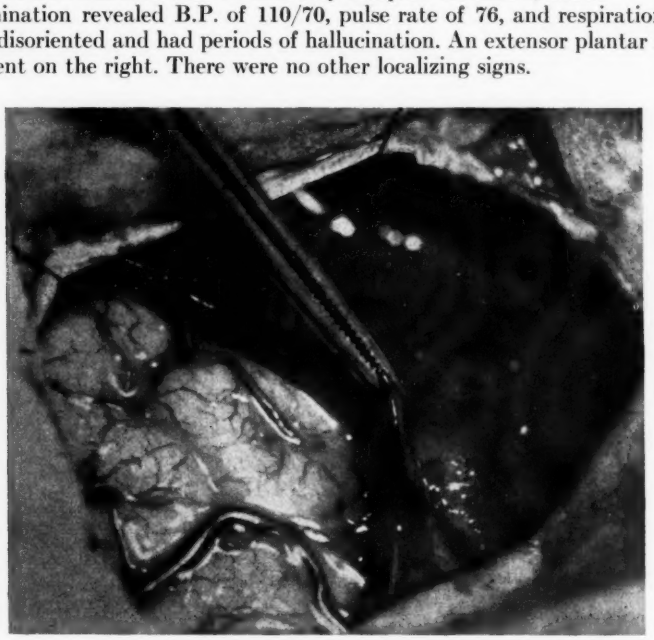

FIG. 4. *Case 3.* Photograph of subdural hematoma over frontal lobe as seen during intracranial trapping of aneursym.

Angiography demonstrated a supraclinoid aneurysm projecting posteriorly from the internal carotid artery several mm. proximal to the bifurcation. There was elevation of both anterior cerebral arteries, more on the left, suggesting the possibility of intracerebral hemorrhage in the region of the corpus callosum (Fig. 3).

The internal carotid artery was ligated in the neck. Six days later this vessel was ligated intracranially (trapping the aneurysm) distal to the aneurysm but below the circle of Willis. A subdural hematoma, with an inner and outer membrane, was found over the right frontal lobe anterior to the intra-aural plane, depressing the cortex 1 cm. from the dura (Fig. 4). At this second operation, the aneurysm was seen to present posteriorly and the sac was thrombosed electrosurgically.

The patient recovered from the operation with a left hemiparesis and 3rd nerve palsy. One year later her physician reported that she was doing well and had only minimal residuals of her original neurologic deficit.

Case 4. H. I. was a 39-year-old, right-handed male who was struck on the head by a steel beam while at work. He had headache and stiff neck for 3 to 4 days. Five months later he had an episode of "flu" following which he had daily headache for 1 month. Twenty-four hours before admission to the hospital, he had sudden onset of weakness and dizziness while fixing a door. He became comatose, Cheyne-

Stokes respirations developed, and blood pressure rose to 240/140. He gradually regained consciousness during the next 24 hours before being referred to University Hospital on May 3, 1951.

Examination revealed B.P. of 110/70, pulse rate of 60, and respirations of 20. Nuchal rigidity was present. The patient was drowsy and confused. Central facial palsy and hemiparesis were present on the left. Extensor plantar response was present bilaterally.

FIG. 5. *Case 4.* Aneurysm of anterior cerebral artery (frontal view).

Lumbar puncture revealed a pressure of 170 mm. of water and grossly bloody fluid.

Angiography was performed after the acute clinical symptoms had subsided. A large aneurysm was demonstrated arising from the right anterior cerebral artery, approximately 2 cm. distal to the bifurcation of the internal carotid artery. There was displacement of the anterior cerebral artery to the left, suggesting an intracortical clot (Fig. 5).

Two days later the anterior cerebral artery was ligated intracranially proximal and distal to the aneurysm. Upon opening the dura, a large acute subdural hematoma of old and bright red blood was found over the right frontal lobe. While this was being evacuated the aneurysm began bleeding and a large subcortical clot

extruded from the frontal lobe under increased pressure. A large clot was also found between the hemispheres and in the left frontal pole.

The patient tolerated the trapping procedure very well and except for a left hemiparesis which gradually disappeared in 1 month, he has no residuals 1 year later.

Case 5. H. W. was a 52-year-old, right-handed male admitted with a 2-week history of right-sided headache. The day before admission a sharp pain developed in the right side of his face and he fell from his tractor. He was seen by his doctor who found him to be conscious and presenting no external injuries except for abra-

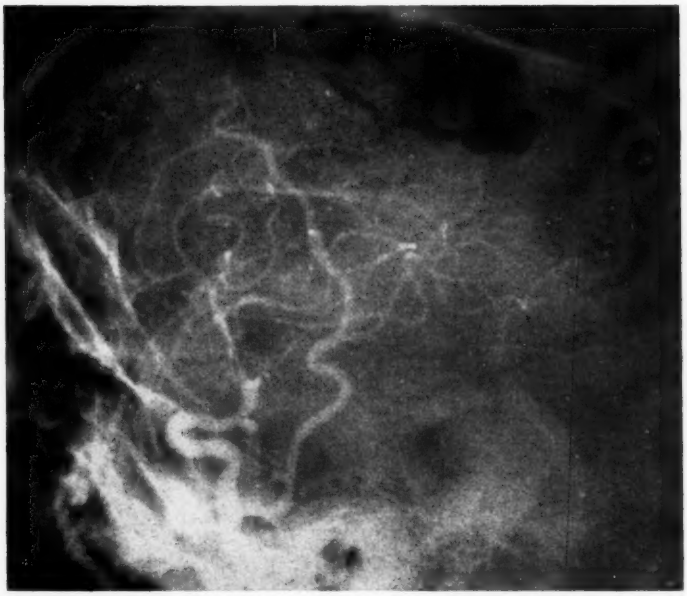

FIG. 6. *Case 5.* Aneurysm of internal carotid artery (lateral view).

sions about the face and neck. He was later referred to University Hospital on Oct. 6, 1951, when he became irrational.

Upon admission there were periods of bradycardia and Cheyne-Stokes respirations. Slight nuchal rigidity was present. He was restless and confused. Pupils were round and equal and reacted sluggishly to light. Superficial and deep pain sensation was decreased over the left half of the body. The left upper extremity showed weakness and forced grasping. The deep tendon reflexes were more active on the left. There was a bilateral extensor plantar response.

X-rays of the skull showed no abnormality.

Under general anesthesia a flap was turned in the right frontal parietal region. A soft fresh blood clot was found in the subdural space. This hematoma depressed the nonpulsating brain 2 cm. from the dura. Subarachnoid hemorrhage was seen beneath this clot. After total removal of the clot the brain pulsated normally.

Ten days later, a small aneurysm of the intradural portion of the right carotid artery was shown by angiography. This lesion was seen to present lateral to the carotid siphon. There was no displacement of the anterior or middle cerebral arteries (Fig. 6).

The internal carotid artery was then completely occluded in the neck with a Selverstone clamp over a 5-day period without ill effects. Two months later a minimal left hemiparesis remained.

DISCUSSION

Subdural hematoma with bleeding aneurysm has been reported by several authors in the study of autopsy material[2,3,6,7,10,11,12,14] but little attention has been directed toward the surgical significance of this condition.[4,5,8,9] Although occurring infrequently in material seen at University Hospital during the period 1941–51 (5 subdural hematomas in 63 cases of surgically treated aneurysm[1]), these lesions presented additional diagnostic and therapeutic problems not common to the usual intracranial aneurysm.

Subdural hematoma in our material was found with aneurysms in various portions of the circle of Willis: 3 intradural carotid aneurysms (1 autopsy case), 2 middle cerebral aneurysms, 1 anterior cerebral aneurysm, and 1 vertebral aneurysm (autopsy case). A lesion of this same type was seen by Hassin[7] in autopsy material associated with an aneurysm of the posterior communicating artery. Autopsy study has disclosed that clot accumulates in the subdural space through tears in the arachnoid.[13]

This group of cases of subdural hemorrhage associated with aneurysmal rupture presented two distinct syndromes. Three cases clinically simulated classical subdural hematoma, and the other 2 cases presented the characteristic story and findings of leaking aneurysm associated with subarachnoid bleeding. A history of significant trauma led to suspicion of subdural hematoma in 3 cases. The studies of Vance[13] on fatal subdural hemorrhage from ruptured arteries suggest that trauma may be an important etiological factor in cases of this type, although the congenital nature may be suggested by an antecedent history of neurological symptoms; such a history may be the initial clue to the surgeon that he is dealing with a more complex lesion than an acute subdural hematoma.

Those cases presenting as bleeding aneurysm were readily diagnosed by angiography; however, the presence of subdural hematoma was not recognized until the skull was opened for attack upon the aneurysm. The presence of subdural hemorrhage was overshadowed by the roentgen signs of intracortical clot.

The diagnosis of aneurysm in those cases presenting as subdural hematoma is difficult. However, certain findings at the time of trephination suggest such a lesion. Following evacuation of the clot, the brain continues under marked tension leading one to suspect the possibility of leaking aneurysm as the source of the bleeding, particularly in the presence of subarachnoid hemorrhage. The presence of xanthochromic or bloody ventricular fluid under pressure or of subcortical clot is further evidence for the presence of

bleeding aneurysm. Aneurysms that manifest themselves clinically as subdural hematoma may be overlooked if the above signs and symptoms are not recognized by the surgeon at the time of evacuation of the clot. When the source of bleeding cannot be visualized through the intracranial opening used in evacuating the subdural clot, aneurysm should be sought for angiographically. Appropriate therapy can then be instituted when the lesion is demonstrated.[1]

SUMMARY

The presence of subdural hematoma with bleeding intracranial aneurysm was found to present additional diagnostic and therapeutic problems not commonly encountered. These subdural hematomas presented two distinct clinical lesions. The clinical findings in one group of cases simulated those of the usual subdural clot. In the other cases the subdural hematoma was discovered incident to treatment for recognized bleeding aneurysm. Upon exposure and evacuation of subdural clot a bleeding aneurysm should be suspected in the presence of subarachnoid hemorrhage, brain under tension, xanthochromic or bloody ventricular fluid, or intracortical clot. When any of these signs are found in association with subdural hematoma diagnostic angiography is indicated.

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PARAGASSERIAN TUMOURS

A. VER BRUGGHEN, M.B., Ch.M.*
Chicago, Illinois

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SMALL tumours near the gasserian ganglion are of interest for several reasons. They may be found unexpectedly in operations for trigeminal neuralgia, and although they are usually meningiomas their surgical removal may be difficult and incomplete. The exact site of origin of meningiomas in this region is not clear. In 1933 Cooper surveyed the literature and reported 76 primary and secondary tumours of the ganglion, while in 1918 Frazier had operated 300 times for trigeminal neuralgia and had encountered only 3. Aneurysm, the other common small space-occupying lesion in this vicinity, can be visualized by arteriography. The paragasserian tumours accidentally found in this group could not have been removed by the posterior approach to the sensory root.

This report concerns 4 cases of paragasserian tumour in the course of 180 operations for trigeminal neuralgia. The diagnosis was correctly made preoperatively in 2, suggested in 1, and unexpected in 1. Three of the 4 were meningiomas, 2 of which were removed; the fourth was a lymphomatous granuloma resembling Hodgkin's disease, also removed. One meningioma was not verified histologically and no attempt was made at extirpation. The patients were women between 49 and 67 years of age. Follow-up was complete.

CASE REPORTS

Case 1. Mrs. S. R., a 60-year-old housewife, was admitted Aug. 28, 1944, complaining of sharp shooting pain in the right nasolabial fold of 6 weeks' duration. A few hours after onset there had been a pain-free interval of a week. At first there was a trigger zone in the labial fold. The pain became continuous and severe and in the last 2 weeks had involved the right eye. Two alcohol injections had failed to give relief and closely placed doses of morphine, gr. $\frac{1}{2}$, had been required to stop the pain.

The past history was noncontributory. The patient's husband had been an invalid for years so that the attending physicians suspected a large functional element in her complaints.

Examination. The patient was emotional and uncooperative. There was hyperesthesia of the 1st and 2nd divisions of the trigeminal nerve on the right which the patient attributed to unsuccessful infra- and supraorbital alcohol injections. Corneal reflexes were equal and motor power in the muscles of mastication was normal. Routine laboratory studies revealed no abnormalities. Roentgenograms showed some cloudiness in the ethmoid and antrum on the right.

Neurosurgical consultation disclosed a history of periodic paroxysmal pain for several years in the right 1st and 2nd divisions. Trigger zones were not found.

* 122 South Michigan Avenue, Chicago 3, Illinois.

Ear, nose, and throat consultation was negative and the sphenopalatine ganglion was injected without relief. The right 2nd division was injected at the foramen rotundum, but pain was present while the distribution of the division was anesthetic.

Course. Throughout the following year the patient was cared for by a colleague in the Ear, Nose, and Throat Department because the neurosurgeon was not satisfied that he was dealing with trigeminal neuralgia.

At neurological examination 1 year later, in October, 1945, the pain was said to be continuous with paroxysmal bursts. The right side of the face was hyperesthetic, the right corneal reflex was diminished and there was slight motor weakness of the 5th nerve. Emotional instability was still evident. The possibility of paragasserian tumour was mentioned.

Operation. On Oct. 15, 1945, a routine temporal extradural approach was made to the right gasserian ganglion. There was more extradural bleeding than expected. A round reddish mulberry-like mass, about 2 cm. in diameter, was found attached to the petrous ridge in the region of the cavernous sinus. The ganglion and the sensory root were pushed downwards, backwards, and laterally by the tumour. It was firmly attached and could not be moved. It appeared to be a meningioma. The sensory root was cut.

Course. There had been no preoperative discussion of tumour and its attendant risks and in view of possible ocular palsy and the imminent death of the patient's husband, it was decided to await developments. Postoperatively there was anesthesia of the entire distribution of the nerve with motor nerve paralysis.

The patient was seen $5\frac{1}{2}$ years later, on March 12, 1951. She felt entirely well and had no complaints. The right side of the face was anesthetic with only slight weakness of the muscles of mastication. Pointed suggestions as to possible headache and diplopia were ignored.

Case 2. Mrs. S. S., a 49-year-old woman, was admitted March 6, 1944, because of sharp shooting pains in the left lower jaw of 3 months' duration. The pain was brought on by eating and there was a trigger point at the angle of the mouth on the left. Spontaneous paroxysms were short, about 15 seconds. The teeth in the left lower jaw had been pulled without relief.

Past history was noncontributory. The menopause had occurred 3 years previously.

Examination. Except for the trigger point on the left lower lip, neurological findings were normal. Routine laboratory findings were not significant.

A diagnosis was made of trigeminal neuralgia of the 3rd division on the left.

Alcohol Injection. The mandibular division was blocked with novocain at the foramen ovale. When the alcohol was injected the whole left side of the face became numb.

Course. The following day examination revealed hypesthesia of the face progressively deeper from above downwards. The corneal reflex was diminished with motor weakness.

In November 1945, 1 year and 8 months later, a simple mastectomy was performed elsewhere. The diagnosis was benign tumour of the breast.

Readmission, June 1946. The patient had had complete relief of pain for 1 year and 9 months. The numbness of the left side of the face had gradually disappeared with the return of severe pain in the face. In the last month the pain had been almost continuous until broken by morphine. The day prior to admission the pain had been continuous for 7 hours.

Examination was impossible; the patient refused to open her mouth or have her face touched. She indicated some residual numbness of the lower division on the left. She had lost 15 lbs. in the preceding month. The temperature was slightly elevated and she was dehydrated. Laboratory findings and roentgenograms of the skull were normal.

Operation. On Feb. 1, 1946, a routine extradural temporal approach was made to the left gasserian ganglion. When the dura propria of Meckel's cave was opened a small tumour, 1.5 cm. to 2 cm. in diameter, was seen to bulge into the defect. The sensory root was cut without identifying the motor root. The tumour was

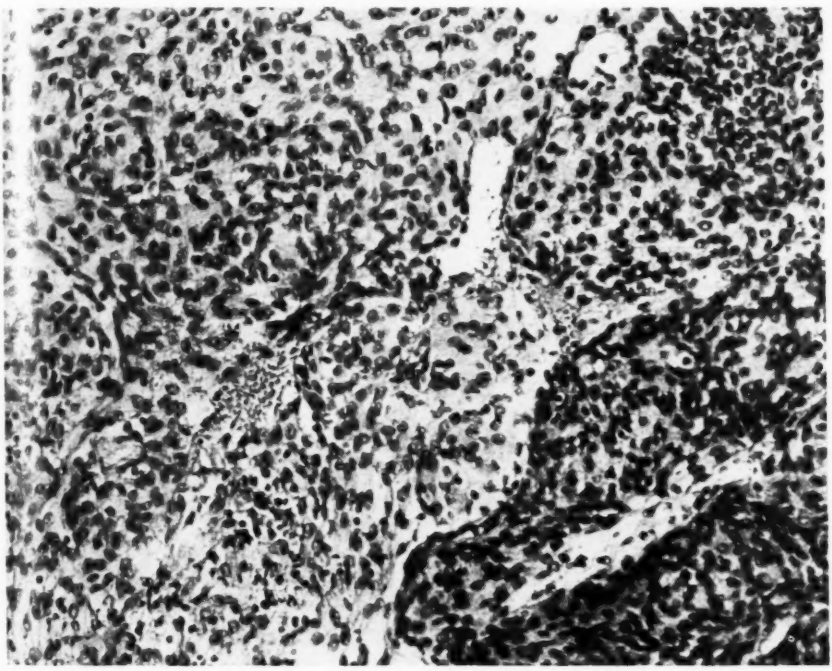


FIG. 1. *Case 2.* The histological picture is that of a meningioma.

then removed piecemeal from its point of attachment on the superior petrosal sinus.

Histological Diagnosis. The tumour was a typical meningioma (Fig. 1).

Postoperative course was uneventful.

At follow-up inquiry it was learned that the patient died Oct. 4, 1946, 8 months after operation. Death was due to adenocarcinoma with metastases to the liver and lumbar spine. The liver weighed 3750 gm. The autopsy was performed elsewhere and the skull was not opened.

Case 3. Mrs. A. M., a 67-year-old Italian woman, was admitted to the hospital from the dispensary Aug. 27, 1949. There was a language difficulty and an interpreter

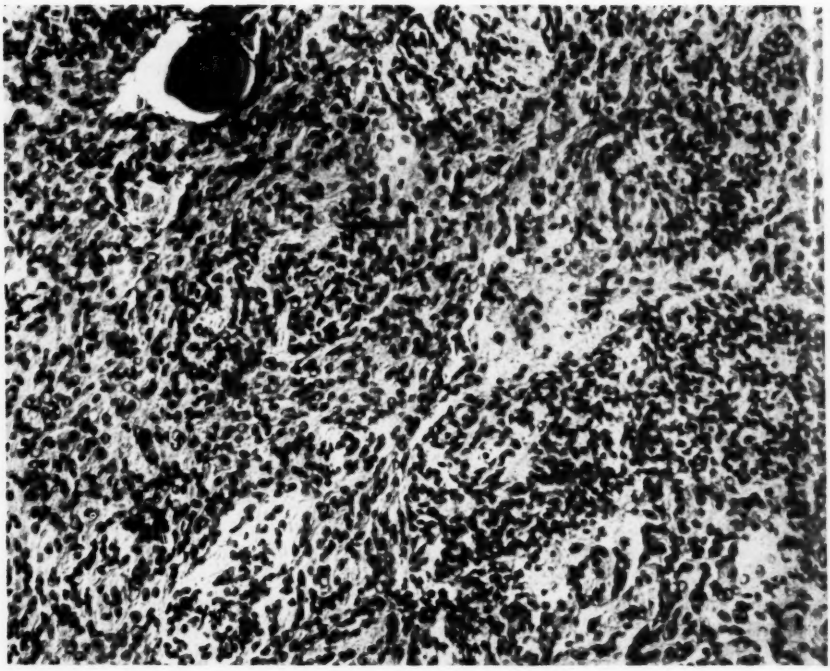


FIG. 2. *Case 3.* The tumour is a meningioma.

and sign language were used. There was a complaint of paroxysmal pain in the ophthalmic and maxillary divisions on the left for 6 years. In recent months there had been a tendency for the pain to be continuous for days. Eating and drinking and laughing precipitated the pain. There was recent loss in weight of 14 lbs. due to diminished food intake.

Examination. There was bilateral chronic noncongestive glaucoma. Neurological findings were negative except for a diminished corneal reflex on the left and hypesthesia of the left side of the face. This was less marked in the mandibular than in the maxillary and ophthalmic divisions. Trigger zones were not obtained and the motor branch was intact.

The changes in sensation in the left 5th nerve led to a tentative diagnosis of paragasserian tumour.

Operation. In August 1949 my assistant, Dr. John Paget, approached the left gasserian ganglion through the temporal route. When the dura propria was incised tumour tissue was found which had pushed the root forward along the petrous ridge.

The tumour was removed piecemeal from its point of attachment to the superior petrosal sinus above the trigeminal impression in the bone.

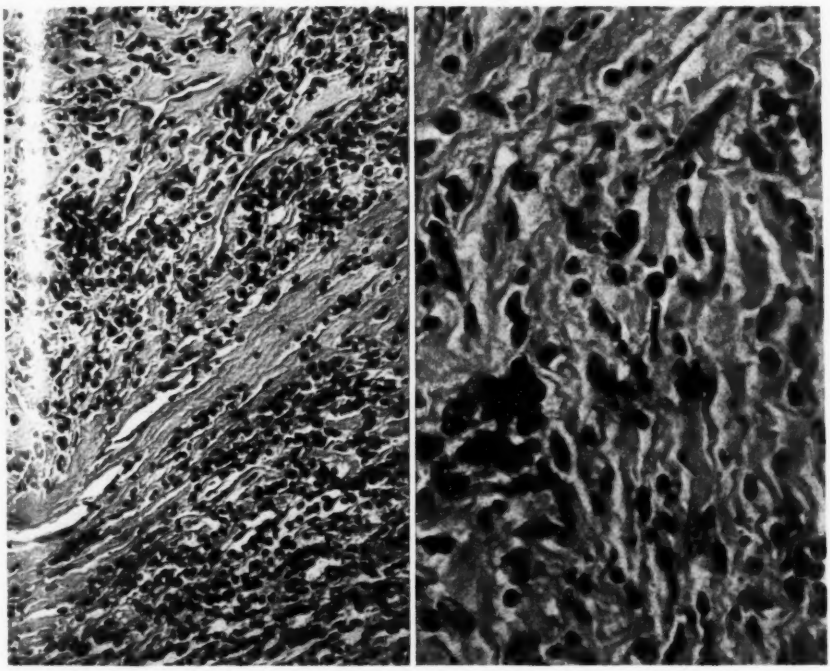
Histological Diagnosis. The tumour was a meningioma (Fig. 2); its size was estimated at 3 cm. in diameter.

Course. Following operation there was complete anesthesia of the left side of

the face with an absent corneal reflex and motor weakness. There was some transient weakness on the right side of the body.

At follow-up in March 1951, the complete left trigeminal anesthesia was noted with slight weakness of the muscles of mastication on the left. She felt very well and had no complaints.

Case 4. Mrs. I. W., a 56-year-old woman, was first seen on May 15, 1950, complaining of pain in the right ear and increasing numbness in the lower jaw. The pain was steady and was associated in her mind with a tonsillectomy performed 2 years



FIGS. 3 and 4. *Case 4.* (*Left*) Lymphomatous granuloma resembling Hodgkin's disease. (*Right*) A high-powered view of this histologically obscure lesion.

before. She felt that she could not bite properly and that food did not taste normal in the right side of her mouth.

Examination. There was diminished sensation to pinprick over the lower part of the right cheek, the inside of the cheek, and the right side of the tongue. Taste was disturbed on the right.

Ear, nose and throat consultation did not disclose anything, but a maxillofacial surgeon felt that there was malocclusion of the right temporomandibular joint. She was treated for several weeks without success.

Course. She returned in January 1951 because of continuous pain in the right side of the face, mainly in the region of the mandibular branch. There was hypes-

thesia in the right side of the face, more pronounced over the lowest division. The right corneal reflex was diminished and there was marked motor weakness. There were hypesthesia and alteration in taste on the right side of the tongue.

A diagnosis was made of right paragasserian tumour. A right arteriogram was considered to be within normal limits.

Operation. On Feb. 26, 1951, the right gasserian ganglion was approached through the usual transtemporal route. After the mandibular division was identified at the foramen ovale, the anatomy became confused. A tumour was identified with its attachment mainly near the foramen ovale with ganglion lying above it. It was

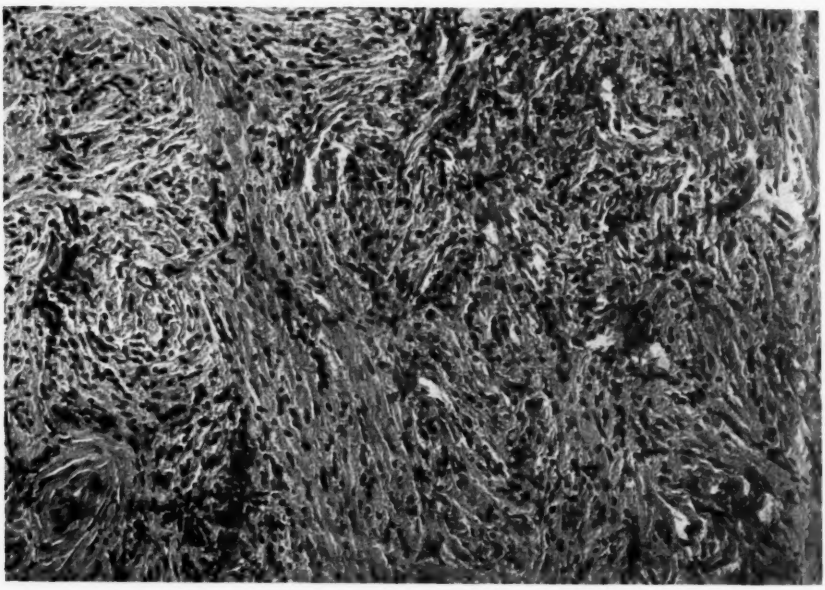


FIG. 5. *Case 4.* The biopsy of the lymph node presented a histological picture similar to that of the paragasserian tumour.

round, greyish-red, nodular and of a firm consistency, measuring about 2 cm. in diameter. The sensory root was divided and the tumour removed piecemeal. The motor root was not seen.

Histological Diagnosis. The tumour is of doubtful origin, but it is probably a lymphomatous granuloma and resembles Hodgkin's disease (Figs. 3 and 4).

Course. Postoperatively there was complete anesthesia of the right side of the face with an absent corneal reflex and motor weakness.

Three months after operation the lymph nodes on the right side of the neck were found to be enlarged. Biopsy was refused. A complete study of the blood showed no definite abnormality. There had been a loss of 8 to 10 lbs. in weight.

In January 1952, the patient lost 10 more pounds, her voice was hoarse, and the nodes on both sides of the neck were enlarged and hard. Examination of the blood revealed no abnormalities. X-rays of the chest and neck were negative. Biopsy of

the lymph nodes revealed a histological picture resembling that of the intracranial tumour (Fig. 5).

Symptomatology. Pain which resembled that of trigeminal neuralgia was the salient feature in these 4 cases. However, its nonparoxysmal character in the late stages was not typical. In 2 there was a complaint of numbness in the face and in 1, disturbance of taste. Weakness of the muscles of mastication was mentioned.

Objective Findings. There were objective findings in all 4 cases. In Case 4 the history and findings were classical and clear. The corneal reflex was altered in 3 cases and in 2 there was diminished sensation to pinprick in the face. Case 2 could not be examined. Trigger zones were not present in the 3 patients who could be tested. Motor weakness was questionable in 2 cases and present in 1. Routine films of the skull did not contribute in any case. Arteriography was done in 1 case and was negative. In none of the cases was there involvement of any cranial nerve except the 5th.

Diagnosis. The diagnosis is based on a somewhat atypical pain in the distribution of the trigeminal nerve with objective findings of impairment of conduction in the nerve. This serves to distinguish it from trigeminal neuralgia, in which the pain is paroxysmal and the conduction of the nerve intact. Difficulty may arise if there has been a previous alcohol injection, following which there may be motor weakness, hypesthesia, and absence of trigger points. The absence of trigger points should make the examiner suspicious. Depression of the corneal reflex is probably the most reliable sign and it is not present in tic douloureux. The cranial nerves must be examined in cases of trigeminal pain. Two patients in this group were treated for atypical facial pain by sphenopalatine injection and other methods. Retropharyngeal malignancy may break through to the vicinity of the gasserian ganglion. The diagnosis must also be differentiated from migraine and herpes. Lesions involving the trigeminal and other cranial nerves do not concern us here. The most common lesion in this part of the skull is the intracranial aneurysm, but other cranial nerves are nearly always involved in addition to the 5th. Angiographic studies should be carried out in suspected cases. Lindgren[14] has discussed the radiographic findings in paragasserian tumours but they probably have attained a larger size than this group to produce them. X-ray films of the skull did not contribute to the diagnosis in this group.

Treatment. This consisted of cutting the sensory root and removing the tumour. I prefer to cut the root first while the field is dry to be assured of relief from pain. Under some circumstances the removal of the tumour might have to be terminated under conditions where visualization of the sensory branch is difficult. In 1 case the root was cut and the tumour was seen but not removed. This patient is still perfectly well 6 years after exploration.

Pathology. Two of the 4 tumours were small meningiomas and a third probably was. The material in Case 4 is difficult to classify from a histologi-

TABLE 1

Paragasserian tumours—4 cases

Date of Operation	Initial Symptoms					Alcohol Injections	Objective Findings						
	5th Nerve Pain		5th Nerve Numbness	5th Nerve Motor Weakness	Other Symptoms		Sensory Loss 5th Nerve	Motor Weakness 5th Nerve	Hyperesthesia 5th Nerve	Trigger Zones	Corneal Reflex Diminished	Impaired Taste	
	Paroxysmal	Continuous											
Case 1 Oct. 1945	At first	Later				+		0 +	+	0	+		
Case 2 Feb. 1946	At first	Later				+		?	+	+			
Case 3 Aug. 1949	At first	Later	+			0	+	0	0	0	+		
Case 4 Feb. 1951		+	+	+	Impaired taste	0	+	+	0	0	+	+	

cal standpoint, but eosinophils and Reed-Stromberg cells were seen, placing it in the category of Hodgkin's disease.

DISCUSSION

It is difficult to estimate the number of primary paragasserian tumours described in the literature because in the accounts of these lesions some of the writers have included secondary tumours. Extension from retropharyngeal malignancy is the commonest. Cushing in his monograph on the meningiomas mentioned a group of these which he called meningiomas of the cavum Meckeli. The tumour "sits like a saddle astride the . . . petrous ridge," producing what he called the gassero-petrosal syndrome. These were much larger tumours than those described here and they produced multiple cranial nerve lesions. They were difficult to remove because they were partly in the middle and partly in the posterior fossa. Incomplete removal and recurrence was the rule, with the result that Cushing adopted a pessimistic attitude concerning them.[3] Tumours of the ganglion sheath, sheath neuroma, neurilemomma, and schwannoma are difficult to classify histologically, and, from the reports, difficult to remove surgically. Fortunately, they are rare.[2,13,18] Epidermoid tumours causing a syndrome resembling trigeminal neuralgia have also been described.[15] Those lesions arising in the sensory root at or near the pons are not germane to this discussion, for they give rise to loss of sensation, cerebellar signs, involvement of other cranial nerves, and increased intracranial pressure, without pain.[9]

The neoplasms that are of most interest here are those giving rise to pain that is indistinguishable at first from trigeminal neuralgia. Secondary tumours, spreading from malignancy in the nasopharnyx, have been men-

tioned and they give rise to a syndrome in which the first symptom is pain resembling tic douloureux.[16,17,20] Fortunately a large proportion of tumours causing tic-like pain are meningiomas, which can be removed with excellent surgical results.[6] However, these also may gain such a size that their complete removal is impossible.[3,19]

That paratrigeminal tumours are rare is attested to by various writers. Cooper[2] in 1933 found 76 cases of primary and secondary tumours of this kind. Davis and Martin[6] in 1939 reported 8 more such cases. Since then only occasional reports have been made, such as that of Love and Woltman.[15] There are probably less than 100 now in the literature. The scarcity of the lesion is further attested to by Frazier's[8] statement in 1918, that, in over 300 operations for major trigeminal neuralgia, he had encountered 3 tumours of the gasserian ganglion. Adson[1] in 1934 had accidentally found only 1 paragasserian tumour in about 600 operations for trigeminal neuralgia. Others have included paragasserian meningiomas in their reports on meningiomas arising anywhere in the cranial cavity.[10,11]

In discussing his reasons for developing the posterior approach to the sensory root of the trigeminal nerve, Dandy[4,5] stated that in over 10 per cent of cases of trigeminal neuralgia, tumour or aneurysm was found in the posterior fossa. Although this statement may be true, none of the tumours described here could have been dealt with through the posterior approach. In 2 of them careful neurological examination did suggest paragasserian tumour; in the other, there was some excuse for its presence being a surprise. Under these circumstances two operative procedures would have been necessary. Dandy gave up the posterior approach during the last year of his life.[7]

The patient with a paragasserian tumour may be erroneously thought to be suffering from trigeminal neuralgia, which may lead to alcohol injection. Case 2 is a striking example of this. The clinical picture was complete with a typical history, trigger zones and relief from alcohol injection. It is hard to know why chemical interruption of a nerve peripheral to its point of irritation should result in relief of pain. Hyndman[12] suggested that oral trigger zones play a most important role in trigeminal neuralgia, and suggested that perhaps denervation of this area would relieve the neuralgia even if the ophthalmic division was involved. Neurological surgeons are aware that the spared ophthalmic fibres may give rise to tic pains at a later date.

SUMMARY

Four patients with paragasserian tumours have been described. Patients with trigeminal neuralgic pain should be subjected to a careful neurological examination with special reference to trigger zones and the corneal reflex. Previous alcohol injection may obscure the value of the test for trigger zones but alterations in the corneal reflex will remain unchanged. The lesion is approached through the classical temporal route with section of the sensory root of the trigeminal nerve, and, if possible, removal of the tumour.

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ELECTRICAL EXCITABILITY OF THE HUMAN MOTOR CORTEX

I. THE PARAMETERS OF THE ELECTRICAL STIMULUS*

MURRAY GLUSMAN, M.D., JOSEPH RANSOHOFF, M.D., J. LAWRENCE POOL, M.D., HARRY GRUNDFEST, Ph.D., AND F. A. METTLER, M.D.

Departments of Neurology and Neurological Surgery, College of Physicians and Surgeons, Columbia University, New York City

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ELECTRICAL stimulation of the human cerebral cortex by repetitive stimuli has long been used by neurosurgeons, but no systematic report has yet been made indicating effective current characteristics in terms of intensity, frequency and pulse duration for a given cortical region in non-epileptic man. By studying these parameters of electrical excitation it was hoped that the optimal type or types of stimuli for a given cortical region could thus be established; that the functions and structural pattern of one cortical region could be more effectively compared with another; and that greater efficiency in locating and mapping the motor cortex and other electrically excitable cortical regions could thus be attained. This last aim was of particular importance in the course of this investigation dealing with psychotic patients in the New York State Brain Research Project since the exact location of the motor cortex was essential as a guide to operative removal of prefrontal cortex.

The induction coil stimulator permitted Ferrier,[7] Beevor and Horsley[2,3,4] and particularly Grünbaum and Sherrington[8,9,12,17] to carry out the basic work of defining and mapping the excitable motor cortex in laboratory animals although neither frequency nor duration of the individual stimuli could be determined. In the classic work of Penfield and Boldrey,[16] use of a thyratron stimulator permitted important correlations to be established between the topography of the human motor cortex and that found by Grünbaum and Sherrington for the anthropoid brain. However, while the thyratron stimulator is technically convenient and is still widely used today, it fails to provide independent variation of duration as well as frequency of individual stimuli, and is limited to stimuli of very brief duration. Excitation with sine wave stimuli, though useful for many purposes (Boynton and Hines[5]) does not provide independent control of the various parameters.

METHODS

The Electrical Stimulation. For the purpose of our studies an electronic square pulse stimulator (designed and constructed in the Department of

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Neurology) offered independent variation of pulse width, frequency and voltage. It provided unidirectional rectangular pulses at an output impedance of 250–300 O., selected in duration in a range from 0.1 to 5.0 msec. and in frequency in the range from 1/2 sec. to 100/sec. As will be seen in a later section, the maximum duration (5.0 msec.) and frequency (100/sec.) proved adequate to define the asymptotes of the strength-pulse width and strength-frequency curves.

The voltage of the stimulating pulses read on an electronic voltmeter,[18] built into the stimulator, was adjustable by an intensity control independently of the other parameters in steps of a fraction of a volt. The stimulator was placed in a control room outside the operating room where it was operated by one of us (M.G.) who recorded all data and observations by means of a two-way communication system. A group of surgical assistants watched and reported all motor responses elicited as a result of stimulation.

Electrode leads carried the stimulus from the control room to the operating room where they terminated in a pair of hand-held bipolar platinum electrodes with the tips 3 mm. apart. These were applied to the exposed motor cortex of the subject by the neurosurgeon. The hand-held electrodes provided the opportunity for frequent examinations of the site of stimulation, the same location being determined by its relationship to surface topography as well as by a silk grid which was placed on the surface of the cortex. Fixed electrodes did not seem satisfactory because continued pressure on a given cortical point as well as unrecognized movement of the point being studied secondary to pulsation of the brain, were undesirable possibilities. To the extent, however, that successive placements of the electrodes were subject to error, our data may have contained minor aberrations. It will be seen in the curves of Figs. 1–6 that these errors were probably small though present. Data obtained in the course of a series of stimulations were repeated and wherever thresholds at the end of the series varied significantly from the initial values, the data were discarded from the results included here.

All observations reported here were made on psychotic patients under general anesthesia. The group studied consisted of 16 schizophrenic patients: 7 of whom were classed as hebephrenic, 5 as paranoid, 3 mixed and 1 catatonic. Pre-anesthetic medication consisted of morphine sulfate, 10 mg., and scopolamine, 3 mg. General anesthesia at the time of operation was maintained with nitrous oxide and intravenous pentothal just sufficient to maintain light anesthesia. The right motor area was stimulated in all cases, and stimulation was always carried out on the intact brain prior to operation upon the cerebral cortex. Cortical points were stimulated for a maximum of 15 sec. but when a response was elicited in less time, stimulation was discontinued immediately upon appearance of a response. An interval of at least 1 min. was allowed between all successive stimulations whether or not they were effective. Studies on a given patient were generally limited to 2 hrs. Occasionally this period was exceeded and in other instances the necessary observations were completed in a briefer period.

Procedure in Determining Cortical Excitability. The *pulse width parameter* was studied at three frequencies of stimulation, 30, 60 and 100/sec. In a given patient a point was selected on the precentral gyrus from which regular and readily observed motor responses were elicited. Then, using the given stimulus frequency and a pulse width of 5.0 msec., the voltage of the stimulus was gradually increased until a threshold level was obtained which just produced a response in 15 sec. of stimulation or less. Maintaining the frequency constant and successively decreasing the duration of the pulses, a series of threshold determinations was then made throughout the entire range of pulse widths permitted by the stimulator. In this manner a strength-pulse width curve was determined for the selected frequency. A series of such strength-pulse width curves at the several constant frequencies in a number of different patients is shown in Figs. 1, 2, 3 and 4.

The *frequency parameter* was similarly determined with the pulse width of the stimulus kept constant at either 1.0 or 5.0 msec. Voltage thresholds were thus obtained at stimulation with the full range of frequencies of the stimulator. The strength-frequency curves so obtained are illustrated in Fig. 6.

RESULTS

The relationship of the parameters of the electrical stimulus to the excitability of the motor cortex was studied in 16 subjects. A variety of cortical points ranging from those giving thumb responses to those giving foot movements were investigated and an attempt was made to study corresponding points in different patients; 16 strength-pulse width curves and 8 strength-frequency curves were obtained. Thus, a total of 24 complete threshold determinations was made as shown in Table 1.

(A) *Threshold and Its Variability.* Since a variety of factors may in-

TABLE 1

Enumeration of investigations

A. Strength-Pulse Width Curves

Series	Stimulation Frequency	No. of Curves	No. of Subjects
1	100/sec.	6	4 (2 subjects have 2 curves each)
2	60/sec.	5	3 (2 subjects have 2 curves each)
3	30/sec.	5	4 (1 subject has 2 curves)

B. Strength-Frequency Curves

Series	Pulse Width of Stimulus	No. of Curves	No. of Subjects
4	5.0 msec.	4	4 (2 subjects also used in series 1)
5	1.0 msec.	4	4 (1 subject also used in series 3)

Total No. of strength-pulse width curves	16	Total No. of all curves	24
Total No. of strength-frequency curves	8	Total No. of subjects	16

TABLE 2

C1-12

Stim. No.	Frequency	Pulse Width (msec.)	Voltage	Time to Response (sec.)	Character of Response
I. Exploration to locate motor points					Start 10:10 A.M.
1	100	5.0	5.8		
2			5.8	4.0	Ext. wrist
3			5.8	7.0	Ext. thumb
4			5.8		Elev. shoulder
II. Excitability measurements on point disclosed in stimulation #3. Strength-pulse width determination. Illustrated in Fig. 1A.					
5	100	5.0	5.8	2.0	Ext. index and thumb
7			3.4		
8			4.3	4.0	Ext. index and thumb
10			4.3	4.0	Abd. index and thumb
11		2.5	3.4		Flex. fingers 3, 2, 4
14			3.4	12	Flex., slt. 2, 3
15			3.4	6	Ext. 2, 3
16		5.0	3.4	7	Ext. 2
20		1.0	5.0	11	Ext. 2, slt. flex. 1
23		0.5	6.6	7	Flex. 3, slt. ext., abd. wrist
26		0.3	7.5	7	Flex. 3, 1, ext. 2
30		0.1	13.0	6	Ext. 1, 2
31		5.0	4.3	7	Ext. 2, flex. 1
34			4.3		
35			5.0	3	Flex. 1, ext. 2
36		0.5	6.6		
37			7.5	8	Flex. 1, ext. 2 End 11:05 A.M.
III. Strength-frequency determination, same point as above.					
40	100	5.0	5.0	7	Ext. 2
44	75		5.8	10	Abd. 1, ext. 2
45	50		5.0	7	Abd., slt. 1
47	50		5.0	9	Abd. 1
48	75		5.0	3	Abd. 1
55	15		17.0		Synch. abd. 1 (slow movement)
59	5		21.5	3	Synch. twitches 1 (major movement absent)
63	1		30.0		Flicker ext. tend. 2
64	100		5.0	3	Ext. 1, 2
IV. Strength-pulse width determination for shoulder point observed in stimulation #4. Illustrated in Fig. 1B.					
65	100	5.0	4.3	2	Elev. shoulder
67			3.4	4	Elev. shoulder, slt.
70		2.5	3.4	14	Contract. delt.
74		1.0	5.0	9	Contract. delt., slt. elev. shoulder
77		0.5	5.8	7	Contract. delt., upper post. arm, slt. elev. shoulder
79		0.3	5.8	14	Contract. delt., lat. head triceps
85		0.1	13.0	9	Contract. post. head triceps, repetitive
87		5.0	3.4	7	Contract. deltoid
88		5.0	3.4	7	Contract. deltoid & lat. head triceps End 12:15 P.M.

fluence interpretation of the data of cortical stimulation, Table 2 brings forward the protocol of one series (Case C1-12) complete except for the omission of stimulations that were ineffective because the strength of the stimulus was lower than any other found effective in this patient. Thus, stimulation #6 (P.W.-5.0 msec.) was omitted from the table because the strength of the stimulus (2.6 v.) was less than that found effective at any time. On the other hand, stimulation #7 (3.4 v.) though ineffective was included because at another time (stimulation #16) this value was effective. In our

TABLE 3

Effect of intravenous pentothal in elevating thresholds

Stimulation Number	Voltage	Response (Extension of Fingers)
Initial Threshold	1.7	+
Pentothal 0.3 gm. given intravenously. Stimulation at approximately 1 min. intervals.		
1	1.7	0
2	2.6	+
3	2.6	0
4	3.4	+
5	3.4	+
6	3.4	+
7	3.4	+
8	3.4	0
9	4.3	0
10	5.0	+
11	5.0	+
12	5.0	+
13	5.0	+
14	4.3	+

studies this occurred occasionally, indicating slight fluctuations in threshold. These variations are indicated in Figs. 1–6 by additional voltage values for occasional points along the curves.

As noted before, when thresholds were erratic, differing significantly at the end of a period of study from the initial values, the data were discarded from the series reported here. Fluctuations in the level of anesthesia were among the major factors influencing such variations in threshold levels. Table 3 illustrates the effect of 0.3 gm. of pentothal, given intravenously, in raising the voltage necessary for a response from a given point, from an initial threshold of 1.7 v. to 5.0 v.

(B) *Variations in the Character of the Response.* The descriptive section of Table 2 also shows the variation of the character of the response from one time to another under the same parametric conditions and under different conditions. In our curves, no distinction is made of these finer variations.

In the 16 strength-pulse width studies, shoulder, thumb, fingers, knee and foot points were investigated and relatively minor variations in response were noted with alterations in the pulse width of the stimulus. The significance of these variations, however, could not be determined definitely because of the possibility of slight errors in the placement of the hand-held electrodes. The 8 strength-frequency studies were carried out on thumb and finger points only. In one instance, from a point giving movements of the thumb at frequencies from 100–15/sec., movements of the face were elicited when the frequency was lowered to 5/sec. In general, lowering the frequency from 100/sec. to 15/sec. or less tended to convert smooth,

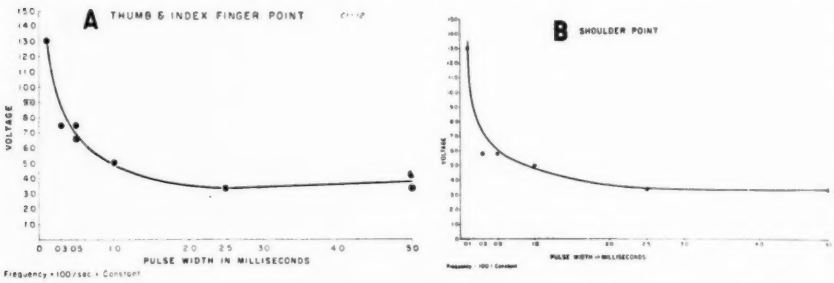


FIG. 1. Strength-pulse width curves for two motor points in the same individual (Patient C1–12). Frequency of the stimulus constant at 100/sec. Threshold intensities in volts are plotted against the pulse width of the stimulus. (A) Motor point for movement of thumb and index finger. (B) Motor point for movement of shoulder.

complete movements of a finger to incomplete twitches synchronous with the stimulus. Other than these findings, however, only minor alterations in response were noted with changes in the frequency of the stimulus.

(C) *The Parameters of Excitation.* (1) The pulse width parameter: Examination of the threshold levels in the strength-pulse width curves shows that at pulse widths of less than 2.5 msec., thresholds rise with increasing rapidity. At pulse widths longer than 2.5 msec., however, the curves are flat or nearly flat and this region constitutes essentially a plateau of constant threshold. Since the onset of the plateau is the same regardless of the three frequencies employed (30, 60, 100), it may be concluded that at any frequency in this range, the most effective stimulus for the motor cortex is one with a pulse width of 2.5 to 5.0 msec. Shorter pulse widths require progressively higher strengths. Longer pulse widths than 5.0 msec. probably do not increase the effectiveness of the stimulus and might cause unnecessary damage.

The strength-pulse width curves have a fairly constant configuration regardless of whether the curves are for different cortical points in the same patient (Figs. 1A and 1B), for corresponding points in different patients (Figs. 2A and 2B), or for different points in different patients (Figs. 1A and

3). Furthermore, the configuration is the same at each of the three frequencies studied (Figs. 1, 2, 3 and 4). Where initial thresholds are higher in one case than in another, the configuration of the curve remains the same but the curve simply moves up along the ordinate indicating that comparably higher strengths are required throughout the entire range of pulse widths (Figs. 4 and 1A).

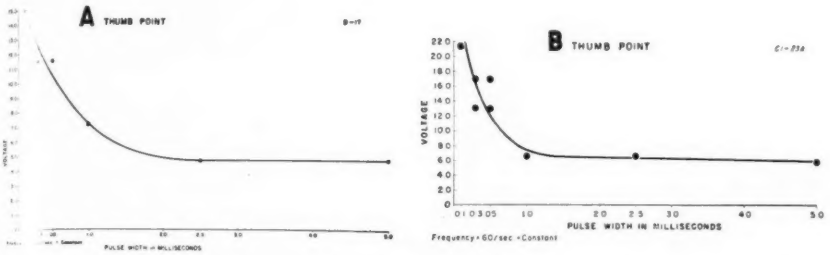
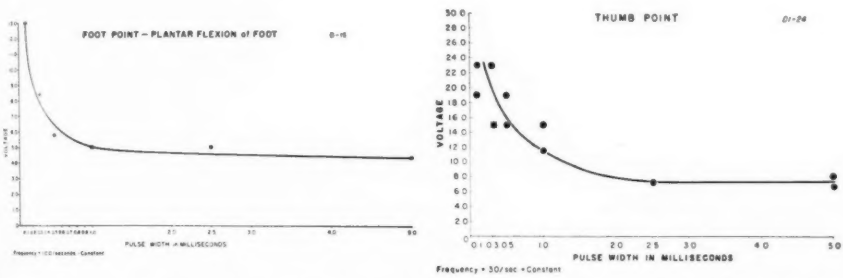


FIG. 2. Strength-pulse width curves for the same motor point in two different individuals. Frequency of stimulus constant at 60/sec. (A) Patient D17. Thumb point. (B) Patient C1–23A. Thumb point.



FIGS. 3 and 4. Strength-pulse width curves in different individuals for the extremes of stimulus frequency and for upper and lower extremities. (*Left*) Patient D15. Stimulation frequency 100/sec. Motor point producing plantar flexion of foot. (*Right*) Patient D1–24. Stimulation frequency 30/sec. Thumb point.

The strength-pulse width curves bear a resemblance to the strength-duration curves of muscle and nerve where single pulses are used instead of the repetitive stimuli employed here, and the plateaus of lowest threshold, beginning at 2.5 msec. in the strength-pulse width curves, resemble the rheobase in the strength-duration curves. Plotted on double logarithmic coordinates, the strength-pulse width curve beyond the plateau, like the strength-duration curve of nerve or muscle, assumes a straight line configuration with a definite slope (Fig. 5). Comparison of the double logarithmic representation of the 16 strength-pulse width curves shows a tendency for the slopes of many of the curves to coincide. Nevertheless, variability in the slopes of other curves is evident. Strength-duration curves for muscle and

nerve show less scatter of the points and much greater uniformity of slope than is observed in the cortical strength-pulse width curves. It must be remembered, however, that the data obtained from the motor cortex represent the results of repetitive stimulation; hence the two kinds of data, while similar, are not strictly comparable.

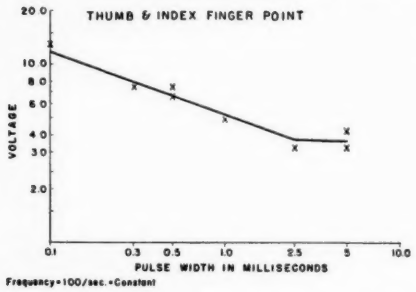


FIG. 5. Patient C1–12. Double logarithm plot of the strength-duration curve in Fig. 1A.

(2) The frequency parameter: The strength-frequency curves also show a rather constant configuration, being similar for different motor points in different patients at either a pulse width of 5.0 msec. or 1.0 msec. (Figs. 6A and 6B). These curves show a progressively rapid rise in thresholds as the frequency of the stimulus is decreased from 75/sec. to 5/sec. and a leveling off in thresholds at frequencies from 75 to 100/sec. Frequencies above 100/sec. were not examined. Nevertheless, the curves suggest that maximal effectiveness is reached in the neighborhood of 75–100/sec. and that frequencies above 100/sec. would not lower the threshold value of the stimulus. On the contrary, it is to be expected that for increasing frequencies the thresholds might again rise, as is the case for nerve and muscle. This effect has been observed by Boynton and Hines.[5]

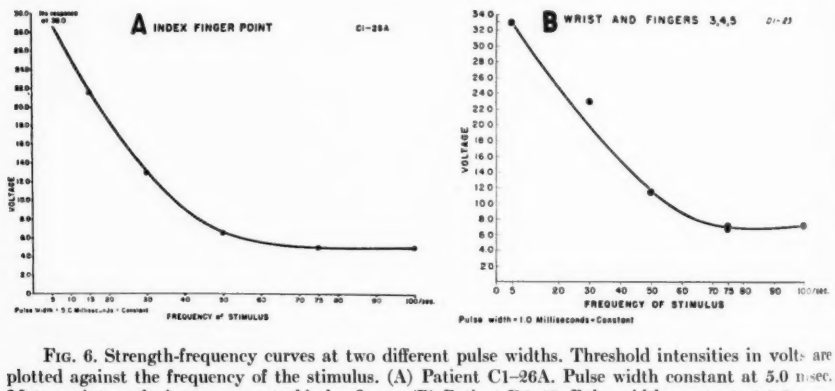


FIG. 6. Strength-frequency curves at two different pulse widths. Threshold intensities in volts are plotted against the frequency of the stimulus. (A) Patient C1–26A. Pulse width constant at 5.0 msec. Motor point producing movement of index finger. (B) Patient D1–23. Pulse width constant at 1.0 msec. Motor point producing movement of wrist and fingers.

DISCUSSION

The above data indicate that in stimulating the motor cortex with square wave pulses the most effective parameters are pulse widths of 2.5 to 5.0 msec. and frequencies of 75 to 100/sec.

The need for definitive data concerning the relationship of the frequency and duration of electrical stimuli to the threshold level of excitability of the motor cortex has long been evident; however opportunities to investigate this relationship have had to await developments in the technique of cortical stimulation. The present data, as far as we know, constitute the first systematic study of this kind on the non-epileptic human motor cortex.

Boynton and Hines,[5] in 1933, employed alternating currents ranging in frequency up to 1440 cycles/sec., to study the relationship of current necessary to produce a given response to different frequencies in the motor cortices of cats and monkeys. Their results were variable: for the cat, the frequency range from 80–120 c./sec. required the lowest voltages; for a 3-day-old macaque, the range was 60–90 c./sec.; while for a 1-year-old macaque, 60 c./sec. was optimal for one point and 90–200 c./sec. was most effective for another point in the same animal. In 1940, Hines[10] reported a similar study using sinusoidal alternating currents ranging in frequency from 5–1440 c./sec. to investigate points on the motor cortex of the chimpanzee. A frequency of 90 c./sec. was found to be optimal, with lower and higher frequencies becoming progressively less effective.

Wyss and Obrador[19] pointed out the fundamental inadequacy of using sine wave stimuli to study the effect of frequency because of the impossibility of altering the frequency without simultaneously changing the duration and shape of each wave. These investigators used double condenser discharges and found that optimum current duration for the motor cortex of the monkey was elicited with a rising phase from 7–20 msec. This corresponded to a full wave duration of approximately 35–100 msec. and considering the shape and duration of each wave, they estimated that optimum frequency for stimulating the motor cortex with alternating current was approximately 25 c./sec. The efficacy of the higher values found by Boynton and Hines was attributed to facilitation. Despite the intrinsic inadequacies of the method used by Hines,[10] the finding that 90 c./sec. is optimal for the motor cortex of the chimpanzee agrees with our results for humans. Further agreement is noted with the work of Liddell and Phillips[13,14] in data published since the inception of our work. These authors stimulated the motor cortex of the baboon with a square wave stimulator and fixed electrodes and found that the optimal pulse duration for single pulses was 5 msec.

Recently, emphasis has been placed on the importance of the parameters of the stimulus in cortical stimulation by observations indicating that the character of the response elicited from the motor cortex, and from cortical autonomic areas as well, depends to a considerable extent on the parameters of the stimulus. Concerning the motor cortex, Bailey and von Bonin[1] noted that responses from the face area of the macaque vary with changes in the characteristics of the stimulus. Liddell and Phillips[13,14] observed that the size of cortical areas representing various movements varied with the parameters of the stimulus and the level of anesthesia. Furthermore, altering the stimulus frequency from single shocks to 50/sec. changed

the motor representation for the same cortex from a map with a few responses of distal parts, covering extensive areas, to the familiar map of fine grain with many responses and narrow areas.

Since our strength-frequency studies were limited to thumb and finger points, we were unable to note the significant changes in the cortical motor representation with alteration in the stimulus frequency as described by Liddell and Phillips. According to the findings of these authors, thumb and finger points, located by exploration of the cortex with a high stimulus frequency, would continue to give similar responses at low frequencies and this is in agreement with our own results.

Concerning autonomic responses, Livingston and Fulton[15] emphasized the importance of the stimulus frequency in obtaining such responses from the frontal area of monkeys and man. Relating the character of the response to the parameter of the stimulus, Delgado and Livingston,[6] from observations on the frontal lobe in the dog and the monkey, suggested that it is possible to elicit from a given cortical point somatic motor effects, respiratory effects, or both, by altering the frequency and intensity of the stimulating current.

Further significance of the parameters of the stimulus in cortical stimulation is achieved by the work of Kaada, Pribram and Epstein[11] who obtained blood pressure and respiratory effects from the temporal pole of the monkey with square wave stimuli and observed that the optimal parameters for stimulation of this region were a frequency of 40/sec. and a pulse duration of 10 msec. These parameters for the temporal pole differ from our findings for the motor cortex and confirmation of this difference would be of importance, indicating that the cortical motor and autonomic areas respond optimally to their own special and different set of parameters. A report on this matter is now in preparation.

SUMMARY AND CONCLUSIONS

Using square wave pulses, the relationship of the parameters of the electrical stimulus to the excitability of the motor cortex was studied in 16 psychotic patients under general anesthesia. Sixteen strength-pulse width curves were determined for a variety of cortical motor points at three stimulation frequencies (30, 60 and 100/sec.) and 8 strength-frequency curves were determined at two different pulse widths (1.0 and 5.0 msec.).

The strength-pulse width curves have a constant configuration, resembling to some degree the strength-duration curves obtained from nerve or muscle and indicate that at a given frequency the pulse width parameter reaches a plateau of lowest threshold at pulse widths from 2.5 to 5.0 msec. in duration. Pulse widths shorter than 2.5 msec. require increasingly higher strength, while pulse widths longer than 5.0 msec. probably do not decrease the threshold value of the stimulus. Similarly, the strength-frequency curves have a constant configuration and they indicate that for a given pulse

width the frequency parameter reaches a region of lowest threshold at frequencies of 75–100/sec.

In stimulating the human motor cortex with square wave pulses, the most effective parameters for eliciting responses were found to be pulse widths of 2.5 to 5.0 msec. and frequencies of 75–100/sec.

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TANGENTIAL WOUNDS OF SCALP AND SKULL*

CAPTAIN PHILIP R. DODGE, M.C., U.S.A.,† AND LT. COL. ARNOLD M. MEIROWSKY, M.C., U.S.A.R.

Tokyo Army Hospital, Tokyo, Japan

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As a result of clinical experience during World Wars I and II, the literature contains many excellent monographs and papers on the subject of craniocerebral trauma from missile-inflicted wounds. The majority of articles have been devoted to the problems of penetrating brain injuries and much less has been written about tangential or glancing wounds of the scalp and skull where the missiles have not penetrated bone and dura. Although seemingly less dramatic than penetrating injuries, tangential wounds present distinct clinical problems; often an apparently simple scalp laceration is associated with considerable disturbance of function of the central nervous system and significant focal pathologic changes. It is the purpose of this report to present observations on a series of patients who sustained tangential injuries, and to describe the method and early results of treatment.

SELECTION OF PATIENTS

During a seven-month period in the Korean conflict, from September 1950 through March 1951, the admissions to Tokyo Army Hospital included 31 patients with nonpenetrating, tangential (grazing, glancing) scalp and skull injuries. These are the case material of this report. Cases demonstrating the penetrating complications of tangential injury with comminuted skull fracture, lacerated dura mater and intracerebral bone fragments, are not included.

OBSERVATIONS

Each patient was examined by one or both of the authors. Skull roentgenograms were taken in all but 1 case. Lumbar punctures, electroencephalograms, and pneumoencephalograms were performed when indicated and technically possible. The average time from injury until the patient was examined by the authors was 14 days, the extremes being 1 and 112 days. Operation, when performed, followed the initial examination by an average of 5 days with extremes of 1 and 30 days. In 2 patients the date of injury was unknown.

ANALYSIS OF DATA

Missile Type.‡ Eight patients reported injury from metallic fragments and 15 from high velocity missiles. There was no correlation between the

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† Present address: Neurological Unit, Boston City Hospital, Boston, Massachusetts.

‡ High velocity missile refers to bullets from rifles, carbines, machine guns and other automatic weapons. Metallic fragment refers to fragments from grenades, mortars and high explosive shells.

results of injury and the type of missile. We could not estimate the speed of the missile at impact. The remaining patients were unable to identify the nature of the missile.

Location of Scalp Injury and Focal Neurologic Signs and Symptoms. Each general region of the scalp was lacerated at least once in the series. Seventeen wounds of the parietal area, 5 wounds of the frontal region, 4 occipital wounds, 3 temporal wounds and 2 combined wounds were seen.

Of the 31 patients, 22 (70 per cent) had focal neurologic signs or symptoms. In 21 of these 22 patients the scalp laceration overlay the region of the cerebrum, damage to which was capable of producing the observed focal findings. A striking feature of these findings was their frequently highly selective nature, such as isolated quadrantopsias and motor and sensory defects confined to a limb or part of a limb. Such findings suggested the superficial nature of the cerebral damage, and the 13 patients with focal signs or symptoms who subsequently came to surgery showed sufficient pathology directly below the scalp lesion to explain the clinical picture just prior to operation. In 5, however, transient initial symptoms, lasting from a few minutes to several hours, had suggested an additional local concussional disturbance of adjacent cerebrum such as that postulated by Russell[9] in a study of superficial gunshot wounds of the head.

Of 9 patients having no symptoms or signs of a focal neurologic deficit 5 had sustained anterior frontal injuries (where small lesions are notoriously hard to localize clinically), 2 had temporal lesions on the nondominant side, 1 an occipital injury, and 1 a posterior parietal injury on the dominant side.

In 17 of the 22 patients who presented evidence of a focal lesion maximal neurologic deficit apparently developed at the time of the injury, while only 2 patients demonstrated progressive focal neurologic signs. Of the latter, 1 had a large subcortical hematoma, and the other a subdural hematoma. No information on the early neurologic findings was available in 3 instances.

Seventeen patients with focal neurologic signs were operated upon and all were found to have severe contusion with either laceration or subcortical hematoma. In addition 3 had venous epidural hematomas and 1 a subdural hematoma. In all of these cases recovery appeared to be accelerated following removal of the lacerated brain and clots. In 3 instances there was no immediate improvement in the neurologic deficit following exploration. These patients had simple contusions which were not attacked surgically. No patients appeared to be made worse by surgery. In 1 case the postoperative follow-up was inadequate.

Five patients with focal neurologic symptoms and signs were not operated upon. In 3 of these recovery was rapid but in 2 recovery seemed definitely delayed as compared to patients with similar findings who were operated upon.

Alteration of Consciousness. Data on alteration of consciousness as determined by post-traumatic amnesia were available in 22 of the 31 cases. Nine (40 per cent) of the 22 patients denied any amnesia, while 13 (60 per

cent) were amnesic for periods of time ranging from an estimated few seconds to 5 hours. The majority believed they were unconscious for a few minutes, although not many could actually document these impressions. No patient with prolonged retrograde amnesia was encountered, and of 8 patients specifically asked, all recalled the sensation of receiving a severe blow of sufficient force to knock them down. One expressed it as: "I felt as though I had been hit over the head with a club." Repeated remarks of this kind indicate the violence of even a glancing blow from a small high velocity missile. When it occurred, loss of consciousness suggested concussion, a widespread reversible physiological dysfunction, in addition to the localized structural lesions. There was no observed correlation between degree of disturbance in consciousness and severity of focal neurologic signs or symptoms. Frequently severe focal symptoms and signs appeared when consciousness had not been altered.

Headache. This was a common complaint and many varieties of headache were described. Data on this point were available in 21 cases. Eighteen patients (85 per cent) experienced headache. Localized aching at the site of injury was noted by 4. Seven complained of generalized or bilateral headache; 3 experienced localized headache at a site distant from the point of injury; 1 had generalized headache after an initial focal headache. One patient had a generalized headache which became focal. The character of the delayed generalized headache in 2 instances was like that seen with tension in scalp muscles and was accompanied by moderately severe post-traumatic symptoms. The duration and severity of the headache varied considerably. Some had headache of short duration and considerable intensity, others described an almost constant aching sensation. Some reported sharp shooting pains, others throbbing pains. Analysis of these data has failed to reveal any significant correlation between the location and character of the headache and the severity of the clinical course. Correlation with pathologic changes was also lacking.

Intracranial Pressure. Evidence of marked, generalized increase in intracranial pressure was uncommon in these patients. Nine (29 per cent) of 31 patients when examined showed some depression of their state of consciousness. In some this was probably related, in part at least, to an elevation in intracranial pressure. Frank papilledema was never seen, although 3 patients had significant blurring of the optic disc margins and 3 others significant engorgement of retinal veins. These signs progressed under observation in 2 instances, but the patients were operated upon before more severe changes appeared.

Fourteen patients had lumbar punctures. In 4 the initial cerebrospinal fluid pressure was between 200–300 mm. of water. A pneumoencephalogram showed significant ventricular shift in 1 of 2 patients who had air studies preoperatively; this was a patient with progressive neurologic signs who was shown at operation to have a large subcortical hematoma. In the only other

case in which there were progressive neurologic signs, the appearance of a 3rd nerve palsy was considered to be due to tentorial herniation of the uncus consequent on a subdural hematoma and increased intracranial pressure.

Seizures. Six (19 per cent) of 31 patients had seizures. All had multiple seizures which began from 3 to 14 days after injury. One patient was seen having generalized convulsions, but the onset was never observed. Of the remaining 5 patients, 3 had lateralized motor seizures which became generalized. Two patients had definite sensory seizures. The latter were associated with spreading paresthesias over one side of the body and never attended by loss of consciousness nor convulsive movements. In each case the seizure began with numbness of the trunk and spread rapidly to involve arm, hand, face, but only occasionally the leg. These 2 patients had parietal lobe pathology on the appropriate side directly beneath the scalp laceration. The exact locus of origin of the fit could not be determined in the 3 patients who experienced lateralized motor seizures, although in every instance the clonic convulsive movements appeared first on the side opposite the scalp lesion, and opposite the presumed or confirmed cerebral pathology. Data were lacking on possible sensory experiences or isolated muscular twitches which may have occurred prior to the more coarse movements.

Surgery was performed on all patients with seizures. Two were found to have only subcortical hematomas. One had a subcortical hematoma with a subdural hematoma. One had a cortical contusion and meningocortical adhesions, and 2 had cortical contusion alone. It should be stressed that in no instance did seizures recur under our observation after operation. No patients received anticonvulsant medication either before or after operation.

Electroencephalograms were available on 2 of our 6 patients with convulsions. Standard 8- and 10-lead electrode placements were employed. One patient had a slow-wave focus localized over the pathologic lesion both preoperatively and postoperatively. The other patient had no EEG preoperatively, but following surgery exhibited a generalized dysrhythmia characterized by scattered bursts of 4–6/sec. moderately high-amplitude slow waves.

EEGs were recorded in 10 other patients who did not experience seizures during the acute phase of their injury. The abnormalities most commonly consisted of a localized slow-wave focus (3–6/sec.) in the region of the scalp laceration.

Roentgenographic Findings. Twenty-two (73 per cent) of 30 patients had no roentgenographic evidence of skull injury. This lack of bony pathology was confirmed in every instance where an operation was performed. Six patients had small depressed fractures demonstrated by roentgenograms. On surgical exploration 1 of these was found to have a depression of the inner table alone, while 2 others had grooving of the outer table and marked depression of the inner table, and 3 had depression of both tables. In 2 cases roentgenograms showed distinct grooving of the external table without de-

pression. This was confirmed at surgery. All the patients with bony damage showed gross lesions of the brain, but equally severe lesions appeared with an intact calvarium.

Surgical Pathology. There were no deaths in this series and accordingly the pathology reported refers to observations made at the time of operation. Various pathologic findings have been referred to in previous sections. In all but 1 (Case 19) of the 19 operative cases there were varying degrees of cortical contusion and laceration. Six patients showed this as the only demonstrable pathology. One patient operated upon several weeks after injury also had a well-formed meningocortical adhesion; 1 had an epidural hematoma; 2 patients had epidural hematomas associated with subcortical hematomas; 2 had subdural hematomas and subcortical hematomas; while 2 had subdural hematomas. Five had subcortical hematomas. All epidural and subdural hematomas cited were of compressive proportions. No histologic studies were made.

The most striking pathologic entity encountered was the subcortical hematoma, which was observed in 9 (47 per cent) of the 19 operative cases. Characteristically, the dura overlying these lesions was tense and when opened the underlying brain was seen to be plum-colored and to bulge significantly. The continuity of the pia was destroyed and frequently the hematomas extruded spontaneously through contused cortex. In no instance did the outer surface of the blood clot lie more than 1 cm. below the cortical surface and both cortex and subjacent white matter were always involved. The actual size of the lesions varied from 2.5 to 4 cm. in diameter. The average volume was estimated at 10 to 12 cc.

*Surgical Management.** Our indications for neurosurgical intervention were:

1) Roentgenographic evidence of a depressed skull fracture.
2) Progressive focal neurologic symptoms or signs.
3) Focal neurologic symptoms or signs persisting with minimal or no improvement for several days.
4) Evidence of increasing intracranial pressure.
5) Seizures.

Frequently several of the above indications existed.

Craniectomy was performed in all but 1 of the 19 operative cases. The exception was a patient without fracture on whom an osteoplastic bone flap was made. The surgical repair of a skin laceration was not referred to as an operative case for the purpose of this paper. However, care was taken to debride and suture all scalp lacerations. The epidural and subdural hematomas were managed in the generally accepted manner. The dura was opened in every instance.The patients with subcortical hematoma and several with

* The surgery was performed by Edward J. Bishop, 1st Lt., M.C., U.S.A.R., Robert A. Clark, Lt. (j.g.) M.C., U.S.N.R., Griffith R. Harsh, III, Captain, M.C., U.S.A.R., Gordon T. Wannamaker, Major, M.C., U.S.A., and the authors.

frank laceration had the blood and necrotic brain tissue removed by a combination of suction and irrigation with copious amounts of saline. The adjacent contused tissue was resected sharply until normal-appearing brain tissue was encountered. Simple contusions were not interfered with at operation. Hemostasis was accomplished by silver clips and/or electrocautery. In the 1 case in which there were meningocortical adhesions, noncytotoxic Gelfoam* was placed between the dura and the cortex after the adhesions were divided. The dura was closed with interrupted sutures of fine black silk. The scalp was closed without drainage.

CASE HISTORIES

The following case histories were selected to demonstrate various features of tangential head injury.

Case 1. F. E. sustained an 8-cm. scalp laceration in the right parietal region near the midline from a high velocity missile which knocked him over. He was dazed but there was no post-traumatic amnesia and he recalled immediate paralysis and numbness of both legs and left arm. Within a few minutes he was able to move his right leg which was functioning normally within 24 hours. The scalp wound was repaired on the day of injury.

When he was examined by us 33 days later his only additional complaint was of an occasional bitemporal headache. He showed complete paralysis below the left knee and a mild, slightly spastic hemiparesis of the entire left side excluding the face. There were increased deep tendon reflexes, absent abdominal reflexes, and extensor plantar response on the left; the right plantar response was equivocal. There was absent position sense in the left great toe and impaired appreciation of number writing over the left foot.

Roentgenograms revealed grooving of the outer table of the skull beneath the scalp laceration.

In view of the severe, persistent weakness of the left leg a right parietal craniectomy was performed 2 days after the initial examination. Grooving of the outer table of the skull was confirmed. Beneath an intact dura there was extensive cortical contusion with laceration of the postcentral gyrus. The Rolandic vein was distended but could be compressed. The liquefied, necrotic zones of cerebral gyri over an area about 2×3 cm. were removed by suction and irrigation. The Rolandic vein remained dilated and the dura was closed.

Within 24 hours after operation there was a 75 per cent return of motor power in the left leg, whereas in the 35 days prior to operation there had been virtually no return of motor function below the left knee.

The patient remained under our observation for 11 days at the end of which time there was only a slight left footdrop. There was no appreciable recovery of sensation in the left foot.

Comment. This case illustrates a number of the characteristic features of this type of injury: the transience of certain initial symptoms, the persistence of signs of relatively severe focal cerebral damage, the unfractured

* Gelfoam is the registered trademark of the Upjohn Company for its brand of absorbable gelatin materials.

skull, intact dura, and severe local damage to the superficial cerebrum. The prompt improvement in motor power so soon after operation would not seem to be coincidental but rather the result of surgical intervention.

Case 15. J. T. was struck tangentially in the left parietal region by a high velocity missile. When seen by us 4 days later, he was complaining of moderately severe bifrontal headache.

Examination revealed a mild right hemiparesis with some increased resistance to passive movement of the long flexors of the fingers and increased deep tendon reflexes on the right side. The plantar responses were flexor. Appreciation of light touch and, to a lesser extent, pain was diminished over the ulnar side of the right hand and forearm. Position sense was impaired in the right ring and little fingers. Skull roentgenograms were normal.

At left parietal craniectomy 1 day after examination the skull appeared normal. There was a venous epidural hematoma, 6 cm. in diameter, with cortical contusion and a subcortical hematoma, 3–4 cm. in diameter, of the postcentral gyrus. The clots were evacuated.

The patient recovered all motor function but the sensory deficit persisted unchanged during 21 days of observation.

Comment. This case shows clinical features in common with Case 1, and also demonstrates other types of pathology. It is included to emphasize the "radicular" type of sensory impairment sometimes seen with superficial cerebral lesions and to illustrate some of the indications for operation. It is of interest that the pathology in this case did not produce more marked impairment of function.

Case 19. C. S. was grazed in the left frontal region by a metallic fragment but remembered no details of his injury when examined 8 days later.

He was lethargic and disoriented. There was a partial 3rd nerve palsy on the left. The fundi were normal. There was no evidence of a skull fracture on roentgenogram.

Three days later the patient seemed less responsive, and bifrontal and left parietal trephinations were performed. A large left frontoparietal subdural hematoma was encountered and removed.

During the next few days there was rapid clearing of the mental state and 38 days later he was discharged. The 3rd nerve palsy cleared gradually and there was no trace of it a few months later.

Comment. This case of subdural hematoma is included to illustrate a different clinical picture and another type of pathology. The presence of local cortical pathology is not excluded in this case; a small frontal lesion is commonly silent clinically and the cortex was exposed through a burr hole only. It was felt that the subdural hematoma adequately explained the clinical picture, and in the absence of seizures or other signs it was felt unjustifiable to perform a more extensive craniectomy.

Case 3. M. S. sustained a tangential, high velocity missile wound of the left parietal area. He was dazed but had no post-traumatic amnesia. His only neurologic

symptom was difficulty in manipulating eating utensils and other small objects with his right hand for a week. About a week after injury he began having a series of generalized convulsions and was transferred to us the next day when the seizures were seen to begin on the right side.

Neurologic examination was negative. Roentgenograms of the skull were normal.

In view of the recurrent seizures a left parietal craniectomy was performed on the day of admission. The skull and dura were intact. The dura was incised and a subcortical hematoma with considerable cortical contusion was uncovered high in the posterior parietal region. The hematoma was removed by suction and irrigation.

There was a temporary supranuclear right facial weakness postoperatively but no further seizures occurred during 32 days of observation. Postoperatively a pneumoencephalogram was normal and an EEG showed nonfocal, generalized bursts of 4–6/sec. moderately high amplitude waves.

Comment. This case illustrates that seizures may be the only symptom of consequence associated with a significant subcortical hematoma.

Case 6. R. T., following a glancing blow in the right posterior parietal region from a high velocity missile, experienced post-traumatic amnesia for a few seconds. He was returned to duty the next day, but 8 days after injury was evacuated because of persistent headache without drowsiness.

When examined by us 15 days after injury, he was symptom-free and the only abnormal clinical findings were blurring of the optic disc margins and a questionable left supranuclear facial weakness. The CSF pressure was 270 mm. of water.

A small depressed fracture beneath the scalp laceration was seen on roentgenogram and confirmed at right parietal craniectomy 6 days after admission. The intact dura was incised and a subcortical hematoma evacuated.

He was discharged 20 days later without symptoms or signs.

Comment. The neurologic symptoms and signs in this case were minimal and operation was undertaken primarily because of the depressed fracture, for a dural penetration with cerebral infection secondary thereto cannot be excluded without inspection. The pathological findings were adequate to explain the moderate rise in cerebrospinal fluid pressure, although it is our impression that ultimately this would have returned to normal without any operative intervention.

Case 9. W. G. sustained a left parietal tangential injury from a missile of undetermined type. Data on alteration of consciousness, if any, are lacking. There were no neurologic symptoms until 1 day after injury when he became dysphasic and a right faciobrachial monoplegia developed.

These signs progressed and were present on examination 6 days after injury. There were no reflex or sensory abnormalities recorded. He was confused as well as dysphasic. Skull roentgenograms were normal, but after admission he had several generalized tonic-clonic seizures. It is suspected that he may also have had seizures prior to the time we first saw him. No papilledema developed, but 6 days after admission a ventriculogram revealed a shift of the ventricular system to the right with depression of the roof of the left lateral ventricle.

A left parietal craniectomy revealed an intact skull and very tense dura beneath which there was cortical contusion with a large subcortical hematoma which was evacuated.

After operation his neurologic signs cleared rapidly and completely, and during the next 16 days there were no further seizures.

Comment. Here the clear progression of neurologic symptoms and signs with distortion of the ventricular system indicated a localized expanding pathology which was confirmed at operation. The hematoma was large and there was probably considerable brain swelling. Again the damage was inflicted through an intact skull, and postoperative recovery was rapid and complete.

Case 12. L. L. suffered a tangential metallic fragment wound of the left occipital region. It is not known whether or not he lost consciousness. He had no neurologic symptoms.

When examined by us 4 days after injury the only sign was a questionable right superior quadrant defect. During his hospitalizations he had 3 seizures beginning with deviation of the eyes to the right, vocal arrest, and then clonic movements of the arms. There was no skull fracture on roentgenogram and a pneumoencephalogram was normal. There was no papilledema but the CSF pressure was 290 mm. and he had severe generalized and retro-orbital headaches.

A left occipitoparietal craniectomy 30 days after admission revealed an intact skull and dura, with cortical contusion, but no laceration or subcortical hematoma. The dura was closed without other operative procedure.

The symptoms disappeared during the next 10 days.

Comment. This patient is included to show that simple cortical contusion and subcortical hematoma may produce the same clinical picture and cannot always be distinguished before operation. Prior to surgery it was felt that this patient had a subcortical hematoma and the finding of a contusion only led us to regard operation in these cases almost as a diagnostic procedure when they showed one or more of the features that have been stressed.

DISCUSSION

Some of the earlier observations pertinent to this report are found in the writings of Jefferson,[7] Cushing,[3] Gamlen and Smith,[5] Horrax,[6] Wagstaffe,[10] Cairns,[2] and Roberts.[8] These authors were impressed, as we have been, with the potential seriousness of this type of injury. However, in our series the mortality rate was nil and quite low mortality figures have been quoted by others. The serious potentiality of the injury lies in the gross disturbance of the cranial contents resulting from a missile injury that has produced slight, if any, bone damage and mild, if any, alteration of consciousness.

The nature and evolution of neurologic symptoms and signs found in patients in this study agree well with similar cases previously reported. Everyone has stressed the fact that the disorder in function can be related to superficial damage to the cerebrum lying directly beneath the scalp wound. As exceptions to this general rule Cushing[3] recorded a case in which death occurred

as the result of a distant hemorrhage in the vermis of the cerebellum, and Jefferson[7] elicited slight, transient signs of contrecoup cerebral injury in 4 of 54 cases of scalp laceration with no bony injury. In our cases transient ipsilateral signs were limited to the foot and leg and were seen only with midline or near midline injuries. This suggested direct rather than contrecoup injury.

The problem of distinguishing clinically between the various types of cerebral pathology may be difficult. When definitely progressive signs and symptoms occur, a space-taking hematoma is almost certain to exist in relation to the dura or superficial cerebrum. The converse is not true, however, and, in this series, epidural, subdural and subcortical hematomas of significant proportions were encountered with persistent but not progressive focal neurologic symptoms and signs. It was only at operation that a definite differentiation could be made between these types of pathology and contusion and laceration. A comparison of Case 12 with those having subcortical hematomas emphasizes this point.

Details of the pathologic findings in our operative cases have been described. In searching for descriptions by other authors we found that Cushing[3] trephined the skull in 38 instances and incised the dura in 11 cases, and although he did not tabulate all of his pathologic findings he described 3 epidural hematomas, a subdural hematoma, and cited some examples of a "plum colored dura" beneath which there was "clot and disorganized brain." Gamlen and Smith[5] in describing the pathology of 6 cases with fits, increasing intracranial pressure, and progressive focal signs, said: "The dura has appeared discolored and unhealthy. Underlying the dura, which was in most cases adherent to the subjacent brain by a layer of altered clot, a considerable cavity containing pulped brain and sanguineous material has been found." Jefferson[7] found extradural clot in 2 of 3 patients whom he trephined. In no instance did he incise the dura but he postulated that meningocortical hemorrhages would be common. Roberts[8] alluded to pulping of the brain with intact dura, but included no details in his report.

As has been mentioned, the epidural and subdural hematomas cited in this report were considered to be of compressive proportions. Quite frequently a smaller collection of blood was discovered above or beneath the dura that was considered to be clinically insignificant.

The pathogenesis of all the superficial cerebral lesions is basically the same, the pathology varying only with the degree of local bruising and hemorrhage. However, the patients with subcortical hematomas and some with severe laceration were demonstrated invariably to have more local swelling and, consequently, greater pressure effects on the adjacent cerebrum than was the case with uncomplicated contusion; in this sense they should be considered space-taking lesions. The absorption of subcortical blood clots is known to be a slow process and it is our definite impression that removal of these clots and of necrotic cerebrum usually effected an accelerated and more nearly complete recovery. The deficit in function related to any part

of the area irreversibly damaged persisted, and presumably improvement resulted from decompression of adjacent cerebrum. Cases 1 and 15 illustrate this point for in both the site of most severe damage was in the parietal region and sensory changes persisted whereas recovery of motor function after operation was rapid.

However, as Cairns[2] has emphasized, the focal neurologic symptoms and signs produced by superficial lesions from gunshot wounds show a strong tendency towards spontaneous improvement. Our experience has been the same but we feel that surgery has value for two reasons. First that, as stated above, recovery is hastened and second that in the presence of a space-taking lesion of any sort, the longer it is allowed to persist the more likely are some irreversible changes to occur in the compressed tissue and the greater will be the persistent loss of function. Cushing[3] was also impressed with the accelerated recovery in his operative cases. He incised the dura less often than he would have liked because of fear of complicating intracranial infection. In this series scalp wounds were widely excised and prophylactic penicillin and streptomycin were used routinely. No case of intracranial sepsis was encountered.

All patients with depressed fracture were operated on, for this is the only way to be sure that the dura is intact. Many cases of depressed fracture, otherwise identical with those here discussed, were excluded from this report by the finding of a torn dura at operation and a direct pathway for infection from the lacerated scalp to the cerebrum. The complicating factor of sepsis makes it difficult to assess the relative importance of mechanical trauma and infection in the production of the clinical and pathologic disorder.

Early seizures were encountered quite frequently in our series (19 per cent).* In a study of gunshot wounds of the head Wagstaffe[10] found the incidence of early seizures to be 5.0 per cent of 224 cases when the skull was fractured and the dura penetrated; 4.8 per cent of 170 cases when the skull was fractured but the dura intact; and 2.5 per cent of 135 cases when there was no bony injury. Jefferson[7] noted Jacksonian fits in 3 of his 54 cases of scalp injury (5.0 per cent). Cushing[3] stated that fits were not uncommon in this type of injury but gave no figures.

It seems reasonable that seizures should be common in tangential injuries where there is such a high incidence of cortical pathology. Originally we felt that seizures meant subcortical hematoma, but in the final analysis this pathologic state was encountered in only half of the patients with seizures; the others had simple contusion.

How surgery influenced the course of these early seizures we cannot say with certainty, for it is well known that they tend to cease spontaneously.[1,4,11] In no case did early seizures continue to occur during the postoperative observation period, and we are inclined to believe that, at least in certain instances, relief of distension of the cerebral tissue was effective in this respect.

* It may be that our seizure figures are too high and reflect an error in selection of cases. Also, there are too few cases in this series for any final conclusions.

With respect to late post-traumatic epilepsy we can draw no conclusions from this series. With only an occasional exception,[11] though, the literature is in agreement that no relationship exists between early and late post-traumatic seizures. It is probable, as Denny-Brown[4] has pointed out, that the mechanism of their production is different.

SUMMARY

The clinical picture and management of 31 consecutive cases of missile-inflicted tangential wounds of the head with intact dura are reviewed and the operative findings in 19 described. Illustrative case histories are presented.

The difficulty of making an accurate pathologic diagnosis before operation is stressed.

The indications for operation are described and the value of operation in these patients is discussed with reference in particular to seizures and to persisting signs of focal damage to the brain.

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CEREBELLAR HEMANGIOMA (HEMANGIOBLASTOMA

A CLINICOPATHOLOGICAL REVIEW OF 40 CASES*

MAURICE L. SILVER, M.D.,† AND GORDON HENNIGAR, M.D.‡

Division of Neurological Surgery and Department of Pathology, Johns Hopkins Hospital, Baltimore, Maryland

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IN THE classical monograph *Tumors Arising from the Blood-Vessels of the Brain*, Cushing and Bailey[4] reported 11 cases of "hemangioblastoma" of the cerebellum. Recent analysis of this cerebellar neoplasm was made by Cramer and Kimsey[3] who presented the clinical findings in a larger series of cases, in 37 of which the tumor was histologically verified. The present paper describes the clinical and pathological findings in 40 cases of this neoplasm, which we prefer to designate "hemangioma" of the cerebellum. We use this term, as others have in the past, in place of the name "hemangioblastoma" proposed by Cushing and Bailey, for reasons that will be presented below.

CLINICAL ASPECTS

There is no predilection for either sex. In our series, there are 24 males and 16 females. The age incidence was from 3 to 62 years of age, the highest falling in two decades, the third and sixth (Fig. 1). The average age was 36.2 years. Only one member of the group belonged to the colored race.

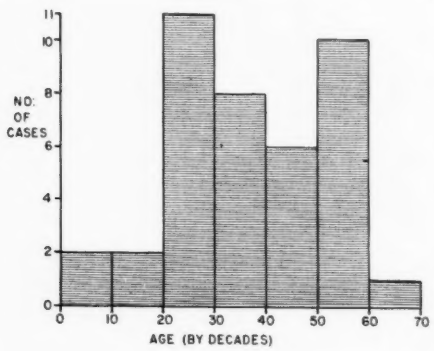

FIG. 1. Age incidence of cerebellar hemangiomas.

The commonest presenting symptom was headache. Other manifestations of an expanding lesion of the posterior fossa were noted, such as ataxia, vertigo, vomiting and blurring of vision. Choked disc was present in 85 per cent of the cases. The average duration of symptoms prior to operation was 10 months.

All of the group were patients at the Johns Hopkins Hospital. Thirty-one were operated upon by Dr. Walter E. Dandy, the remainder by other attending or resident surgeons of the hospital staff. In view of the va i-

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† Present address: 224 Thayer Street, Providence, Rhode Island.

‡ Present address: Department of Pathology, Medical College of Virginia, Richmond, Virginia.

ation in surgical technique, a detailed analysis of mortality is not warranted.

The operative mortality for the group was 20 per cent, 2 patients dying shortly after admission before operation could be performed. Of the 30 patients surviving surgery, 7 are now dead, having had an average survival period of 10.7 years; the life expectancy in this group, as computed from actuarial tables, is 37 years. At least 2 of the patients died from causes unrelated to the tumor. Twenty-three patients are still alive and their average survival to date is 6.2 years. The 5-year survival rate, commonly applied in the analysis of tumor surgery, is 50 per cent.

Nine of the 40 patients were subjected to more than one operation, 2 patients having had four operations. It is not clear whether these reoperations were performed because of independent isolated foci manifesting themselves at a later date, or because of continued growth of incompletely removed tumor tissue.

The late appearance of hemangiomas of the central nervous system in Lindau's complex is well known. In our series, 9 patients had proven Lindau's disease, 4 of them requiring multiple operations. This figure of slightly more than 20 per cent in our series of cerebellar hemangiomas agrees with that of Lindau, who found that 20 per cent of the patients with retinal hemangioma (so-called von Hippel's disease) subsequently were shown to have a cerebellar neoplasm or other evidence of Lindau's complex. It raises the serious possibility that all patients with a cerebellar hemangioma are suffering from Lindau's disease in which other members of the pathological complex have not yet appeared.

In the diagnosis of the cerebellar hemangioma, clinical laboratory examinations are of limited value. The cerebrospinal fluid protein seldom is elevated and then only minimally. This is in contrast to the spinal hemangiomas, with which it is exceedingly high. The explanation for this probably lies in the fact that the former are seldom in contact with the subarachnoid space, whereas the spinal lesions almost invariably involve this space.

In examination of the peripheral blood, we found that 40 per cent of these patients had hemoglobin values greater than 15 gm., and in 3 cases values as high as 18.5 gm., with a red blood cell count of 6.3 million, were noted. In none of the cases were blood and plasma volume determinations, arterial oxygen saturations, or bone marrow studies performed, yet in these 3 cases, the clinical diagnosis of polycythemia rubra vera was made and treated by venesection.

PATHOLOGICAL ASPECTS

Hemangioma of the cerebellum may be cystic or solid, single or multiple, and situated either in the midline or in the hemispheres. Forty per cent of the tumors showed attachment to the meninges, half of these (8 cases) to the dura, usually to the ventral aspect of the tentorium. Thirty tumors consisted of a nodule with a single large cyst, 4 had a grossly multiloculated cystic appearance, and 6 were solid.

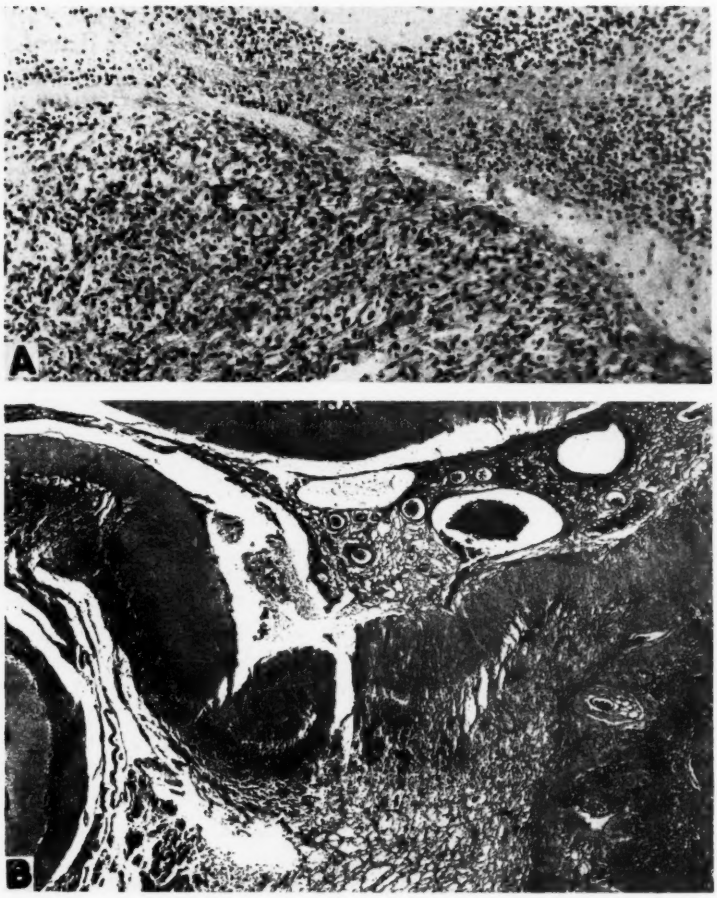

FIG. 2. (A) Relationship of a juvenile-type hemangioma to granular layer of cerebellar cortex. H&E, ×100. (B) Growth of tumor in subarachnoid space and white matter of cerebellum. Zone of cleavage between cerebellum and hemangioma is demonstrated. H&E, ×30.

Grossly, the majority of the tumors were circumscribed and demarcated from the adjacent cerebellar tissue by a loosely arranged network of glial fibers. This line of demarcation facilitates the removal of the tumors, the superficially placed ones being readily "shelled out" (Fig. 2).

There is considerable variation in the diameter of the cyst. The latter is usually filled with a yellow to brown, gelatinous transudate. Protein values when measured were as high as 5.5 gm. per cent. The mural nodule may be situated in any location in the cyst wall and varied from 0.5 to 5 cm. in diameter. When small, it may be difficult to locate at surgery. Large, pron i-

nent, patent or thrombosed, thin-walled vessels may be seen coursing over the surface of the cyst. Seldom is the pia mater or dura mater thickened or firmly adherent to the cyst, so that meningeal attachments of the tumor are readily divided.

We propose the following histological classification: (1) juvenile type; (2) transitional type; and (3) clear-cell type.

(1) The *juvenile type* is predominant in the first three decades of life and is characterized by the presence of thin-walled capillaries lined by endo-

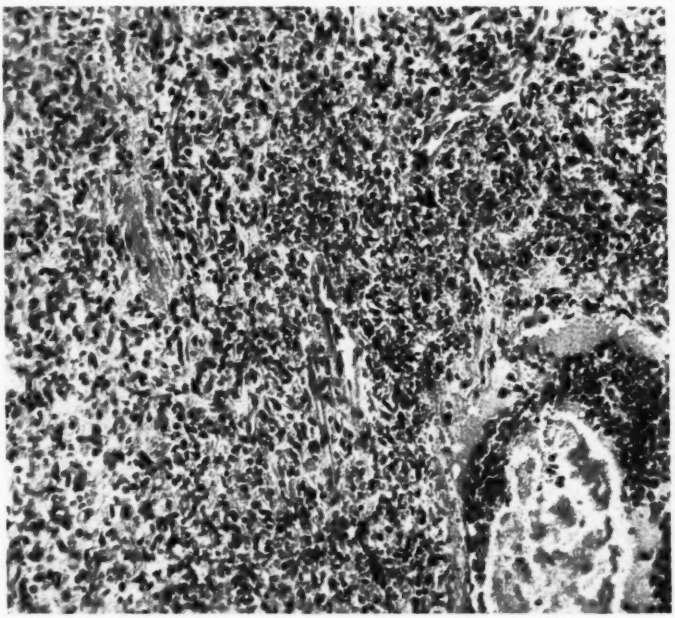

FIG. 3. Capillary-cavernous juvenile-type hemangioma. H&E, ×200.

thelium. There is a varying number of dilated vessels and tightly packed capillaries (Fig. 3). Around these capillary-cavernous and blood-filled spaces, one sees a protein coagulum which is most likely transuded plasma (Fig. 4A). This plasma is precipitated by the fixative and in some cases may be abundant, forming a halo of pink-staining finely granular material about the vessels in the hematoxylin and eosin stained sections.

Between the blood vessels are sheets and strands of endothelial cells, identical with those lining the vascular spaces. These cells almost invariably show no variation in size, shape, and staining qualities. Prominent nucleoli and mitotic figures are almost never seen. Mononucleated or multinucleated giant cells are rarely evident (Fig. 4C).

We have chosen the name "juvenile" for this capillary-cavernous he-

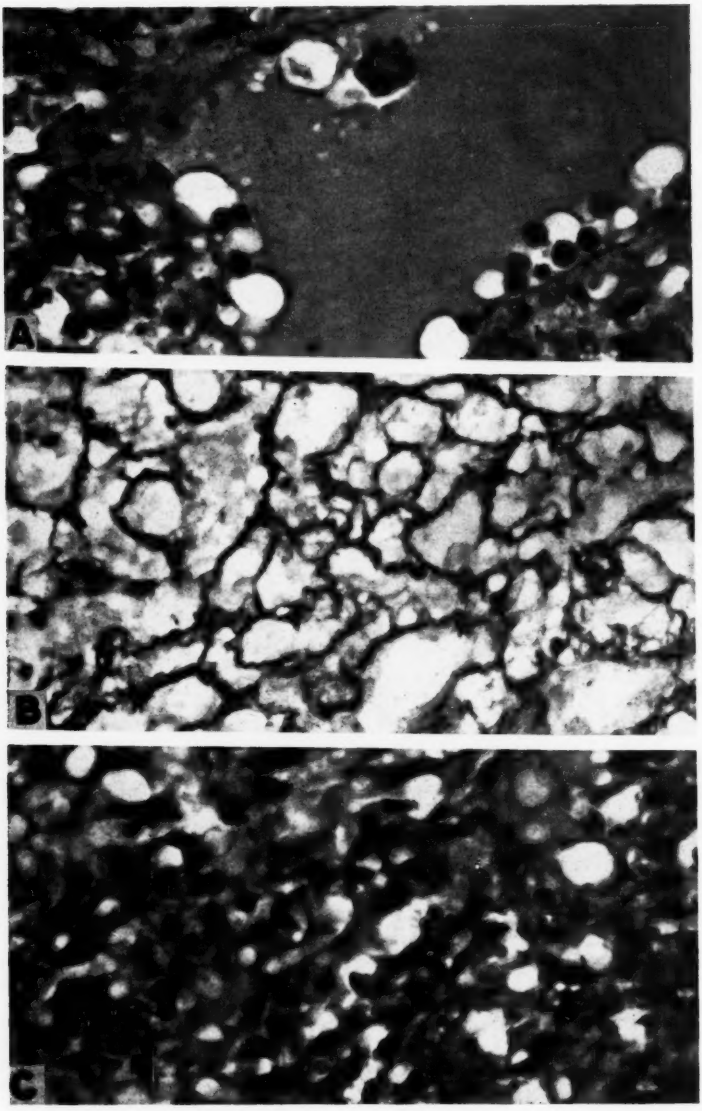

FIG. 4. Juvenile-type hemangioma. (A) Protein coagulum in intercapillary space (microcyst). H&E, ×600. (B) Capillaries, outlined by reticulin. Reduced silver, ×600. (C) High power view of cell types. H&E, ×600.

mangioma, not only because it occurs in the younger age groups, but because microscopically it represents the earliest picture designated by the term "hemangioma," that is, a benign tumor forming blood vessels. As will be described below, this uniform and monotonous picture changes with time, and the development of hemorrhages, transudates, cyst formation, and periods of rapid growth. Some authors[1] have suggested that with the passage of time, the neoplasm undergoes a sclerosing and obliterative process. In our material, we have failed to demonstrate by special stains the development of abundant connective tissue between the vessels, comparable to the scleros-

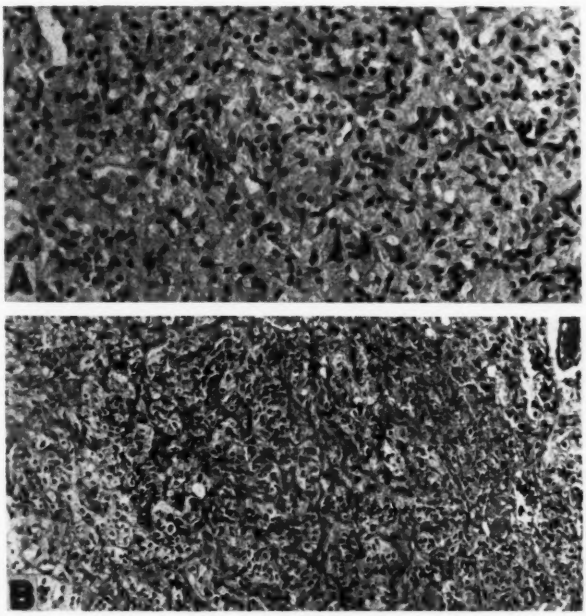

FIG. 5. Transitional-type hemangioma. (A) Endothelial cells with pale-staining cytoplasm. Occasional large nuclei or multinucleated cells are present. H&E, ×200. (B) There is wide variation in size and shape of endothelial cells, and suggestion of alveolar arrangement of clear cells. H&E, ×100.

ing type of hemangioma of the skin. Instead, silver stains reveal abundant reticulin adjacent to the capillary walls (Fig. 4B).

(2) *Transitional type.* With the development of hemorrhages within the tumor, there is a response on the part of the endothelial cells. They undergo hyperplasia and utilize their phagocytic power to engulf the red cells and coagulated serum. They swell up and become filled with sudanophilic (lipid) material. This takes the form of large globules and finely dispersed lipids. These xanthoma cells then have a clear or pale-staining cytoplasm, with a centrally placed nucleus. The presence of lipids in the cell cytoplasm was confirmed by utilizing tissue fixed in 10 per cent formalin, cutting frozen sec-

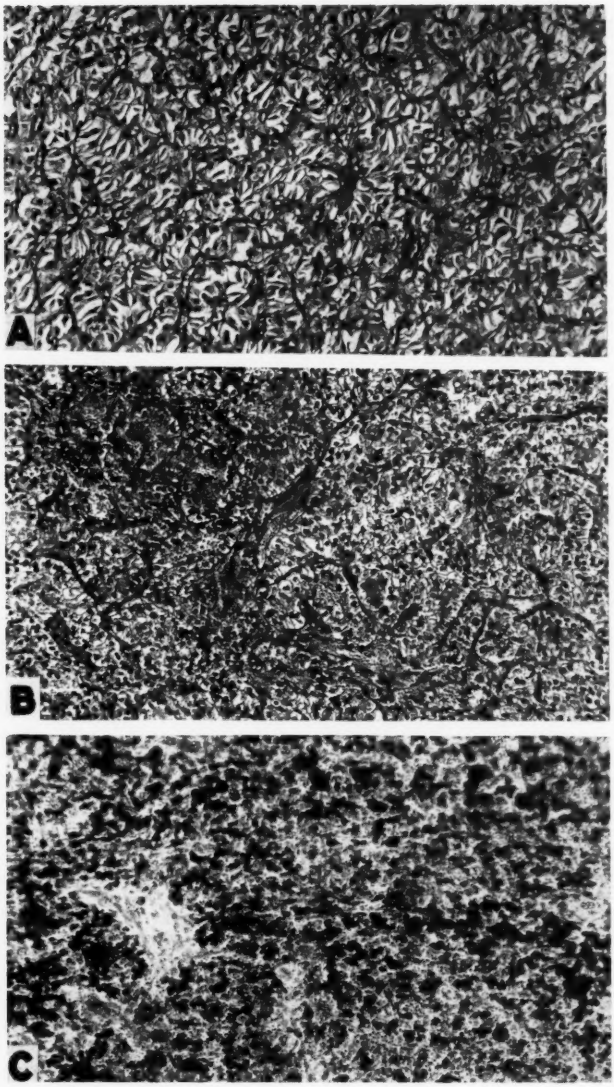

FIG. 6. Clear-cell type hemangioma. (A) Pseudotubular (alveolar) arrangement. The entire tumor showed this uniform appearance. H&E, ×100. (B) Another example, with the cells separated by a reticulin framework. H&E, ×100. (C) Frozen section of tumor in (B) stained for fat. Dark granules are sudanophilic. Sudan IV, ×100.

tions, and staining them with Sudan IV. In this category, the term "transitional" was chosen to signify a transition from the juvenile to clear-cell type. The absence of cytoplasmic staining appears to be the result of the extraction of engulfed lipids in the routine preparation of hematoxylin and eosin sections. In this type, a few to moderate numbers of large mononucleated giant cells appear, microcysts become prominent, and there are areas of hemorrhage. Thus, the uniform appearance of the juvenile type is lost (Fig. 5).

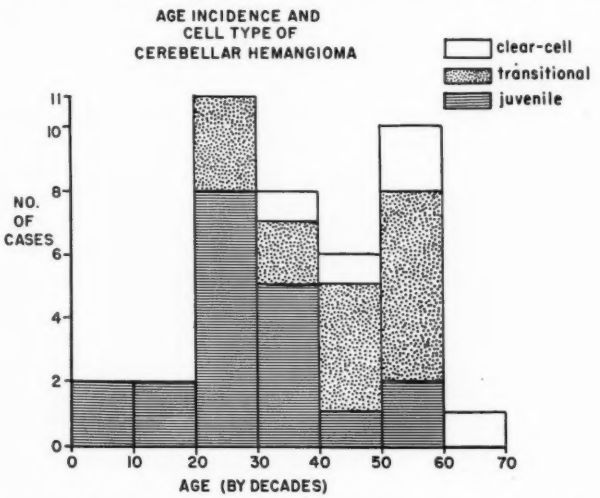

FIG. 7. Correlation of age of patient and cell-type of tumor in 40 cases of cerebellar hemangioma. The predominance of the juvenile type in the younger age groups, and the transitional and clear-cell types in the older age groups is noted.

(3) *Clear-cell type.* The last category comprises the group in which the neoplasm is made up *almost entirely* of xanthoma cells (Fig. 6). In our series, these tumors occurred with but one exception in the older age groups. In several of the patients who had "recurrences," a change from juvenile type, through transitional cell, to clear-cell type was noted.

Histologically, the usual pattern is one of sheets of cells with a rich vascular stroma. In some of the tumors, however, there are pseudotubular formations around a blood vessel. Giant cells and abundant microscopic cysts become prominent.

The microscopical picture is to be differentiated from that of a metastatic hypernephroma. In this regard, mitotic figures and prominent nuclei may prove of value in the diagnosis, as they do not occur with significant frequency in hemangioma but are common in the more undifferentiated types of hypernephroma. However, it appears very difficult, if not impossible, to distinguish clear-cell hemangioma of the cerebellum from the well-differentiated types of metastatic clear-cell hypernephroma.

The correlation of the various histological types with the ages of the patients is shown in Fig. 7. It may be noted that the second peak of incidence corresponds to a predominance of transitional and clear-cell forms of the tumor occurring in the older age groups.

DISCUSSION

The diagnosis of hemangioma of the cerebellum should be considered in every patient presenting signs or symptoms of an expanding lesion of the posterior fossa.

As emphasized by Lindau,[5] and Cushing and Bailey,[4] the presence of a cerebellar neoplasm in a patient with (a) familial history of angiomatous disorder or (b) evidence of involvement of another organ, as seen in Lindau's complex, permits the pre-operative diagnosis of this neoplasm. The patient's age may indicate a reasonable estimate of the degree of differentiation of the tumor.

The fact that this cerebellar neoplasm, when occurring as an isolated tumor, is indistinguishable from the cerebellar hemangioma of Lindau's disease, raises the possibility that a similar etiologic factor, heredofamilial in nature, underlies this condition.

There has been considerable speculation in the literature (most recently by Tonning, Warren, and Barrie[6]) regarding the etiology of the neoplastic transformation in this vascular tissue. They regard it as a "fundamental persistent lack of integration between blood vessels and parenchyma." We concur in viewing the disease as a dynamic process superimposed upon a heredofamilial developmental defect. The chronological transition of the tumor from juvenile to clear-cell type describes a life-history for this neoplasm which lends itself to logical classification. This classification is offered in place of the previously used "solid" or "cystic" categories, the latter referring to a presumed coalescence of smaller cavities into a larger cyst.

Our conception of the growth-potential of these neoplasms ascribes to them a limited capacity for proliferation. We note the infrequency of mitotic figures, the loose cellular structure, the increasing deposition of hemosiderin and lipids, and the late appearance of mono- or multinucleated giant cells, all as evidence of low or absent cytological malignancy. For these reasons, we feel that the term "hemangioblastoma" conveys a false conception of malignant potentiality and primitive structure for a tumor that we believe to be more appropriately classified as "hemangioma," a benign tumor of adult tissue.

In all of our cases, save one, there has been no evidence whatsoever suggestive of hematopoiesis within the tumor. An intensive search for erythropoiesis in all sections from the entire series was unsuccessful in demonstrating such foci, except in a single case in which polycythemia rubra vera had not been ruled out.

The relationship between cerebellar hemangioma and so-called polycythemia has been noted by a number of authors.[2,3] There is no satisfactory

explanation for the occurrence of an elevated red cell count in the peripheral blood in association with cerebellar hemangioma. It is interesting, however, that a high incidence of erythrocytosis has not been noted with any other intracranial lesion. Review of a large series of astrocytomas by the authors failed to disclose any erythrogenic tendency. Further hematologic studies are required to evaluate this erythrocytic tendency in association with other vascular tumors of the brain. (The term erythrocytosis seems preferable to polycythemia, as the latter implies neoplasia of the erythropoietic tissue, for which the term polycythemia rubra vera is reserved.)

The clinical manifestations of cerebellar hemangioma are but little dependent upon the specific nature of the growth, and largely dependent upon the location and size of the lesion, especially with respect to obstruction of the ventricular system. Treatment, therefore, is entirely a neurosurgical problem, with subsequent irradiation having no clear-cut effect upon the course of the illness.

In our histological studies, we have not been impressed with multicentricity of the lesions as stated by Cramer and Kimsey.[3] It would seem likely that "recurrence" of the tumor is the result of incomplete removal, whether caused by mechanical failure of complete removal at the operative site, or failure to recognize adjacent tumor tissue. The latter is always a possibility due to the wide variation in gross appearance of hemangiomatous tissue. Complete removal, which is frequently difficult, should not be followed by "recurrent" tumor.

The development and significance of the clear-cell type of cerebellar hemangioma is worthy of emphasis because this type may be confused microscopically with metastatic hypernephroma of the kidney by the pathologist unaware of its characteristics.

SUMMARY

The cerebellar hemangiomas are benign, usually cystic, but occasionally solid neoplasms which may become manifest at any age. Surgical removal offers an excellent prognosis.

The relationship to Lindau's disease, as well as to erythrocytosis, should always be investigated in the hope of throwing further light upon the interrelationships among these conditions.

The varied histological appearance of the cerebellar hemangioma should be recalled so as to avoid a mistaken diagnosis of a malignant or metastatic lesion.

The analysis of 40 histologically verified hemangiomas of the cerebellum permits classification of these lesions as juvenile, transitional or clear-cell in type, based upon the stage of development of the tumor.

This paper is dedicated to Professor Percival Bailey, on the occasion of his 60th birthday.

We wish to express our appreciation to Drs. A. E. Walker and A. R. Rich for their constant encouragement and kindness in reviewing this work.

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TRAUMATIC INTERNAL CAROTID ARTERY THROMBOSIS SECONDARY TO NONPENETRATING INJURIES TO THE NECK

A PROBLEM IN THE DIFFERENTIAL DIAGNOSIS OF CRANIOCEREBRAL TRAUMA

RICHARD C. SCHNEIDER, M.D., AND LLOYD J. LEMMEN, M.D.

Department of Surgery, Section of Neurological Surgery, University of Michigan Hospital and Medical School, Ann Arbor, Michigan

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IN PATIENTS who have concomitant injuries of the head and neck the physician's attention is directed to the cranium when neurologic symptoms are present. This is particularly true when the trauma to the neck is of a blunt nonpenetrating type, and the neurologic manifestations simulating severe craniocerebral injury are not recognized as arising from thrombosis of the internal carotid artery. We wish to report 2 such cases recently encountered which demonstrate the challenge that this type of lesion presents to the physician in diagnosis and treatment.

While only an occasional case of thrombosis of the carotid artery secondary to nonpenetrating injuries of the neck has been reported in the literature, the presence of embolism or thrombosis associated with penetrating wounds of the neck or cheek has been more frequently recognized,[2,3,4,11,16,17,18,21,24,27,28,34] especially in war wounds of the last century.[32] In addition,[13] since cerebral angiography has been used more widely in the diagnosis of neurological abnormality, certain patients with no apparent trauma are found to have a spontaneous carotid artery thrombosis.

Verneuil (1872)[33] was probably the first to report a case of thrombosis following a nonpenetrating injury of the neck:

> His patient had been found under a railroad car in an agitated and shock-like state. Examination disclosed a contusion to the vertex of the skull, ecchymosis of the groin, and a 5–6 cm. perineal laceration. During the next 24 hours a right hemiplegia and profound coma developed, and the "contour of the left sternocleidomastoid muscle was effaced by a swelling." A diagnosis of hemorrhage of the brain was made. Postmortem examination 5 days after the injury demonstrated the following findings. The brain appeared grossly normal. Thrombus formation in the left internal carotid artery was found about 2 cm. distal to the bifurcation of the common carotid artery. While the external wall of the vessel was intact, the intima and the media at this point were torn so that their edges were rolled under, forming a nidus for thrombus formation. The thrombosis extended into the most peripheral branches of the middle cerebral artery. Cut section of the brain revealed softening of the left cerebral hemisphere. Verneuil postulated that there had been a sudden wrenching of the neck with no blow directly to the artery because there was no contusion or hematoma. He emphasized the importance of the differential diagnosis "between diverse accidents that can follow traumatic lesions of the head."

In 1935, Greco[11] reviewed the literature on injuries to the carotid artery in the neck with thrombosis, and listed 22 cases in which this phenomenon occurred secondary to penetrating wounds of the face and neck. To these he added another case of thrombosis of the internal carotid artery that followed a nonpenetrating injury to the neck:

While riding his bicycle, a 23-year-old male was struck by a horse-drawn carriage which knocked him down, but he did not lose consciousness. He was dazed and had no recollection how the trauma had occurred. Although the patient was able to continue his bicycle ride, shortly after the episode he had transient generalized malaise and blurring of vision. These symptoms subsided only to recur again an hour later with headache and vomiting; later he became unconscious. Bradycardia and a right hemiplegia developed about 16 hours after the accident. Examination revealed superficial abrasions over the left chin and lower lip. No anisocoria was noted; the right cremasteric and right patellar reflexes were absent, but a right extensor plantar reflex was elicited. Palpation of the carotid vessels in the neck was not performed. Lumbar puncture was normal. A diagnosis of possible left middle meningeal hemorrhage was made. Left temporoparietal craniotomy revealed no abnormality except minimal pulsation of underlying brain. Postmortem examination 60 hours after injury disclosed encephalomalacia of the left cerebral hemisphere. A small hematoma was found over the left carotid sheath just to the left of the thyroid cartilage. No extravasation of blood into the neck was seen. At the origin of the internal carotid artery a linear transverse laceration was noted which had involved the intimal and medial layers of the vessel and there was retraction of their margins for a distance of 8 mm. Strongly adherent thrombus at this site had greatly reduced the lumen of the vessel, and at the level of the foramen lacerum the vessel was completely occluded by this process. The thrombus extended into the branches of the internal carotid artery.

Moniz,[19] in 1941, presented a case of severe trauma to the head which was so marked that traction on the carotid artery apparently tore the intima and resulted in a thrombosis to the vessel.

In 1944 Northcroft and Morgan[22] presented a case of traumatic thrombosis:

A young soldier was walking along the road when a lorry passed him. A loose rope hanging from the vehicle wound around the patient's neck, throwing him to the ground, and then rapidly unwound itself without dragging the patient. He did not lose consciousness, and was able to walk to a nearby dispensary where a single stitch was placed in a superficial scalp laceration in the right parietal area. A contusion was observed on the left side of his neck. On the following day the swelling in the left sternocleidomastoid area was larger; right Jacksonian seizures and a right hemiplegia developed. Roentgenograms of the skull showed no fracture. A left extradural hemorrhage was considered. A burr hole in the left side of the skull revealed only "healthy brain." The left lateral ventricle was tapped and the pressure was normal. The patient died 19 hours after operation. Postmortem examination revealed external marks of the rope on the neck. Two-thirds of the left sternocleidomastoid muscle was found to be ruptured. The left internal carotid artery contained a thrombus which extended into the middle cerebral, part of the left anterior cerebral, and the left posterior communicating arteries.

There is some question whether Case V reported by Erikson[10] should be included in this group or be classified under spontaneous thrombosis of the internal carotid artery with coincidental head trauma:

For several years a 28-year-old male had suffered from periodic headaches. He sustained a blow to the head which was followed in a few hours by increasing apathy and a flaccid left-sided hemiplegia. Right carotid angiography demonstrated obstruction in the internal carotid artery just below the base of the skull. Subsequent postmortem examination revealed an adherent thrombus, 2 cm. long, in the internal carotid artery at this point. Distal to this point was a thrombus, 3 cm. in length and reddish gray in color, lying free from the vessel wall. A large cerebral infarct was found in the right cerebral hemisphere.

Closely associated with nonpenetrating wounds of the neck are minor lacerations with carotid thrombosis as illustrated by Case 4 of Caldwell and Hadden:[2]

A 20-year-old male was injured when his truck overturned on an ice-covered highway. Following a lucid interval he became comatose 4 hours after injury. Examination disclosed a (1) compound comminuted fracture of the right mandible near the angle, (2) simple fracture of the left clavicle, (3) superficial laceration of the anterior triangle in the right neck. Five hours following injury the jaw fracture was reduced. Skull roentgenograms showed no fracture. The left eyelid was ptosed and there was twitching in the left facial muscles. The left leg and arm were paralyzed.

Exploratory trephines revealed normal dura and cortex. Thirty-four hours after injury the patient died. Autopsy revealed a thrombosis of the right common, external and internal carotid arteries.

CASE REPORTS

We would like to report 2 cases of internal carotid artery thrombosis which occurred secondary to nonpenetrating injuries to the neck and simulated epidural or subdural hematoma.

Case 1. L.O., a 42-year-old right-handed white female, was involved in an auto accident at 10:00 A.M. on March 19, 1951. She was thrown out of the car as it overturned; the vehicle struck the right side of her head. It was not possible to ascertain whether she had been unconscious; however, on arrival at a local hospital she was conscious and it is alleged that she was able to move her left upper extremity but not the lower extremity. When she became progressively more lethargic, she was referred to the University Hospital 12 hours later with a diagnosis of "acute head injury."

Examination disclosed a B.P. of 120/70, respirations of 28, and pulse rate of 120. Abrasions and contusions were observed lateral to the right orbit, in the right supraclavicular region, and anteriorly over the right chest. There was a palpable fracture of the right clavicle. There was dullness to percussion over the left chest and breath sounds were reduced over the left base. The patient was lethargic but was well oriented. The miotic pupils were equal. There was forced conjugate deviation of the eyes toward the right (Fig. 1) with inability to move the eyes to the left of the midline. During the 12 hours following injury a complete left hemiplegia

had developed with a left extensor plantar reflex. Roentgenograms of the skull showed no fracture. Further roentgenography showed fractures of three ribs of the right chest, and fractures of the right clavicle (Fig. 2) and the pelvis. There was a right pneumonitis with hemothorax. Urinalysis showed no abnormality.

Ophthalmodynamometric study revealed the retinal artery pressures to be 25/40 O.D. and 65/115 O.S. Lumbar puncture disclosed a pressure of 180 mm. of water, 5 WBC, and a total protein of 80 mg./100 cc.

Course. A right stellate block with 10 cc. of 2 per cent procaine was performed with no change in her hemiplegia.

On the following day open arteriography demonstrated an occlusion of the right

FIG. 1. *Case 1.* There is conjugate deviation to the right and a right facial weakness. The dressing covers the incision made for the right carotid arteriography. Contusion over the right clavicle is not readily visualized.

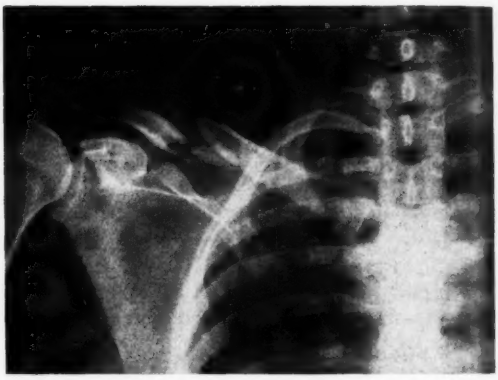

FIG. 2. *Case 1.* The site of fracture of the right clavicle is demonstrated.

internal carotid artery 3 cm. distal to the bifurcation of the common carotid. There was reflux filling of the right vertebral artery during the injection (Fig. 3). Definite transmitted pulsations were observed in the exposed segment of the internal carotid artery. Superior cervical sympathectomy was performed at the time of angiography with excision of 3–4 cm. of the chain and ganglia.

Five days after the angiography conjugate deviation of the eyes to the left of the midline was possible. Three months later marked emotional lability, left hemiplegia with a left extensor plantar reflex, and left homonymous hemianopsia were present.

Comment. The differential diagnosis in this case rested between an expanding extra- or subdural hematoma, a right frontal intracerebral hematoma, cerebral fat embolism to the smaller vessels of the right frontal lobe with infarction, and thrombosis of the right internal carotid artery. This-

proportion between the patient's alertness and orientation and severe neurological deficit did not suggest an intracranial hemorrhage. Her vital signs and her state of consciousness did not indicate the presence of a rapidly expanding intracranial lesion. The diagnosis of fat embolism could not be established.[26] The diagnosis of internal carotid thrombosis was made clinically because of the right supraclavicular contusion, the relatively alert state of mind initially compared to the degree of neurologic disability, and the differences in the retinal artery pressures. The diagnosis was confirmed by carotid angiography.

FIG. 3. *Case 1.* Right internal carotid arteriogram. The arrow indicates the site of thrombosis of the right internal carotid artery. The external carotid artery was strangulated with a rubber drain, and there has been reflux filling of the right vertebral artery.

Case 2. P.H., a 24-year-old right-handed white male, was injured in an automobile accident at 1:00 A.M. on Nov. 23, 1951. He was semiconscious when first examined, and a left hemiplegia developed with deepening coma during the next 36 hours. He was admitted to University Hospital at 3:00 P.M. on Nov. 24, 1951.

Examination revealed a B.P. of 195/100, pulse rate of 62–84, and respiratory rate of 20 per min., irregular. There were multiple abrasions of the right side of the neck, face, and forehead. The right lower extremity rested in a Thomas splint with marked swelling of the middle third of the thigh. On auscultation there were a moderate number of extrasystoles, and moist rales were heard at both lung bases. The patient was semicomatose but responded to painful stimuli with movement of the right side of his body, and only slight movement of the left. There was hypertonicity with hyperactivity of deep reflexes on the left. Abdominal and cremasteric reflexes were absent on the left, and extensor plantar reflexes were elicited bilater-

ally. The right pupil was larger than the left, but both reacted to light. Funduscopic examination revealed blurred disc margins bilaterally with distension of the retinal veins. The carotid pulse was palpable bilaterally in the neck.

Roentgenograms of the skull displayed no fracture, but there was a fracture of the middle third of the right femur. Urinalysis revealed a trace of albumin and many fat particles by staining techniques. A tentative diagnosis of right extradural hematoma was made.

Course. Burr holes were made over the right temporal, frontal, and posterior parietal regions. Upon incising the dura there was a herniation of the brain at each burr hole. An unsuccessful attempt was made to tap the right ventricle from the posterior parietal trephine opening. Another burr hole was therefore made at the homologous site on the left side; upon tapping the left ventricle the cerebrospinal fluid escaped under markedly increased pressure. Ventriculogram showed a shift of the left lateral and 3rd ventricles from right to left; there was no air visible in the right lateral ventricle (Fig. 4). Right percutaneous carotid arteriography on three injections demonstrated a thrombosis of the internal carotid artery about 3 cm. above the bifurcation of the common carotid (Fig. 5), with filling of the external carotid artery. Because of the pronounced cerebral edema a Penfield type of subtemporal decompression was done on the right and a Cushing procedure on the left. Upon incising the dura there was a marked herniation of the brain through the dural openings. A Kirschner wire was placed through the right tibia to immobilize the fractured right femur. A polyethylene catheter was inserted under the carotid sheath and a continuous procaine block of the cervical sympathetic chain was carried out[23] using 1 per cent xylocaine.

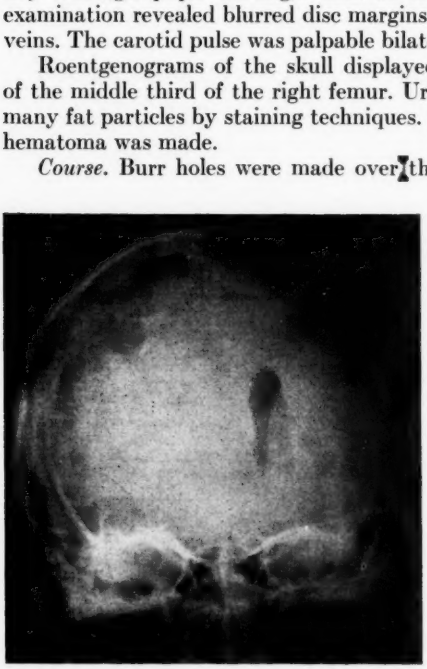

FIG. 4. *Case 2.* Ventriculogram showing partial filling of the left lateral ventricle with none on the right. There is also a pronounced shift of the entire ventricular system from right to left.

Prior to operation multiple particles identified as peanuts were recovered by intratracheal suction, and thick mucopurulent material was aspirated frequently postoperatively. For 12 hours after operation the blood pressure remained at 120/90 and then gradually fell to shock levels despite all attempts to maintain it with blood and vasopressor agents. The pulse continued to be rapid and thready. The temperature rose to 105 F. and the patient succumbed at 8:00 P.M. on November 25.

Postmortem Examination. There were numerous abrasions on the forehead over the orbits, below the left eye, and over the bridge of the nose. Moderate swelling was present on the right side of the neck beneath the mandible. There was an extravasation of blood into the right sternocleidomastoid muscle, and around the carotid sheath of the common carotid artery in the region of the bifurcation. The needle puncture of the previous arteriography was 4 cm. proximal to the lowermost

point of the extravasation. The right carotid artery was occluded just proximal to its bifurcation by thrombus (Fig. 6). This thrombus extended into the anterior, middle and posterior communicating arteries. Convolutions of both cerebral hemispheres were flattened and hyperemic with more pronounced swelling and marked ecchymosis over the right frontoparietotemporal cortex (Fig. 7). Distinct right tentorial and cerebellar pressure cones were found. Section of the brain showed diffuse softening of both gray and white matter with multiple infarcted areas in the right cerebral hemisphere. An 80 per cent atelectasis was observed in the right lung. Crepitus was palpable over the right femur.

FIG. 5. *Case 2.* Right common carotid arteriogram demonstrating filling of the external carotid branches in the neck and thrombosis of the internal carotid artery about 3 cm. above the bifurcation.

Comment. There are several important lessons to be learned from this case. The patient presented the clinical picture of acute increased intracranial pressure. There was the failure primarily to consider thrombosis of the internal carotid artery in the differential diagnosis. An expanding intracranial lesion was suggested by the dilated right pupil and the bilateral extensor plantar reflexes indicating the formation of a tentorial pressure cone. Since no surface lesion could be demonstrated by burr holes and no intracerebral hematoma in the right hemisphere could be localized by the ventriculogram, an arteriogram was made thereby demonstrating the thrombosis

of the internal carotid artery. Diagnosis in this instance could be made only by the dye study, since there was no demonstrable change to palpation of the carotid pulse in the neck.

The marked cerebral edema could have been due to cerebral hypoxia secondary to the thrombosis and an almost complete atelectasis of the right lung. Continuous stellate block was employed to promote the collateral arterial supply and increase oxygenation of the hemisphere. In retrospect an

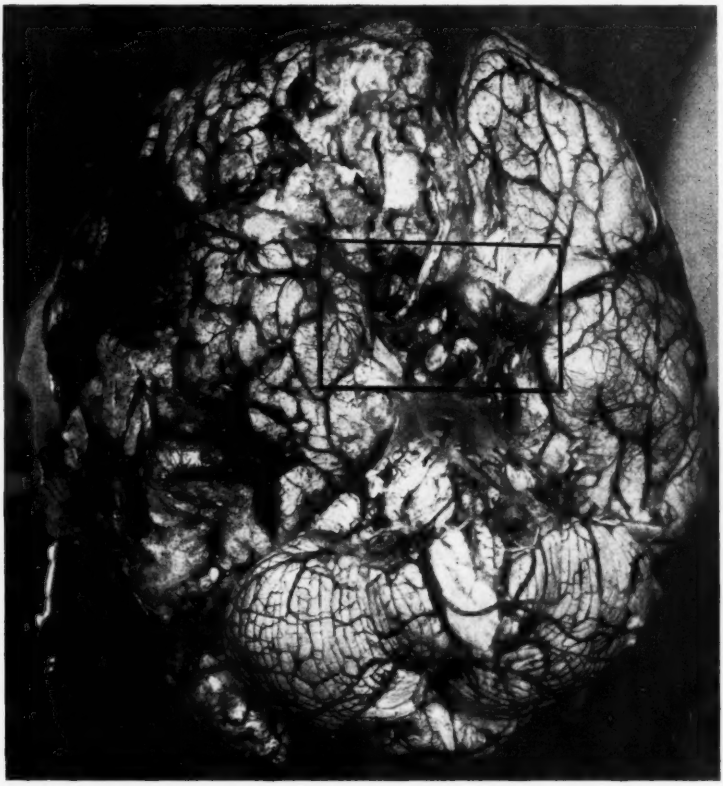

FIG. 6. *Case 2.* Postmortem specimen showing the severe edema and ecchymosis of the right cerebral hemisphere. See Fig. 7 for magnification of outlined area.

early bronchoscopy and tracheotomy probably would have been of aid in maintaining better aeration of the lung, and might have increased the patient's chance of survival.

PATHOLOGY

Legal limitation in the autopsy examination prevented microscopic examination of the bifurcation region of the common carotid artery. Studies of Verneuil,[33] Greco,[11] and Caldwell and Hadden[2] showed that there was a tear

in the intima with associated damage to the media and a curling up of these layers to form a nidus for thrombus formation. The first author believed that this was due to a wrenching movement of the neck with no direct trauma to the vessel, but Greco regarded the blow to the vessel as the etiological factor. Arteriosclerotic changes may be contributing factors to forma-

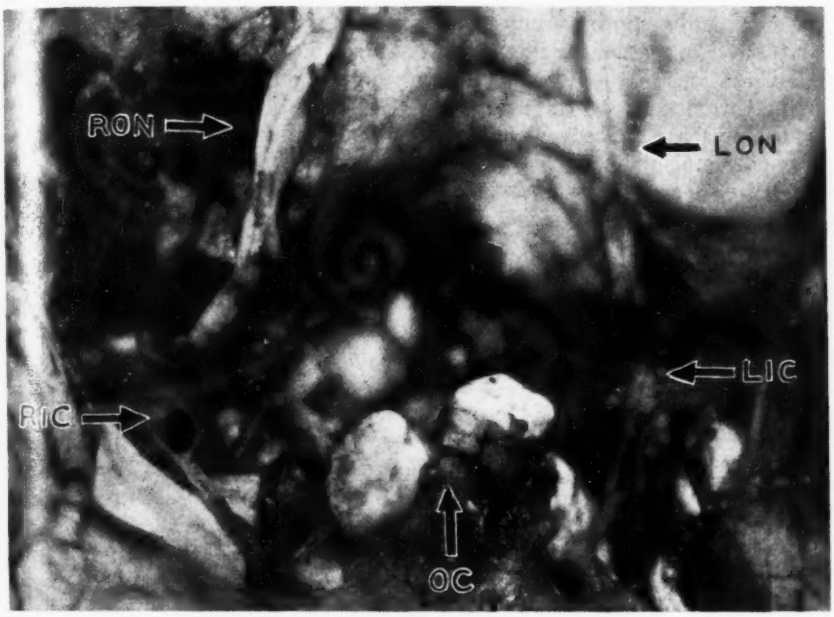

FIG. 7. *Case 2.* Magnification of outlined area in Fig. 6. RIC, right internal carotid artery. LIC, left internal carotid artery. RON and LON, right and left olfactory nerves. OC, optic chiasm. The thrombus is seen in the right carotid artery.

tion and propagation of thrombus. Associated with injury to, or near, large arteries is spasm involving some part of the artery or entire arterial beds. Spasm in the artery as well as in the arterial bed is usually caused by abnormal reflexes since extensive arterial thrombosis is not a common finding in the initial stage of this syndrome.

Ecker[7,8] has described a syndrome of spasm of the internal carotid artery. It consists of: (1) dysfunction of a cerebral hemisphere, (2) brain swelling in the acute stage, (3) internal hydrocephalus in a late stage and (4) narrowing of the cerebral arteries. He presented 4 cases which illustrate the association of this syndrome with nonpenetrating wounds of the neck and blunt injuries of the head.

DIAGNOSIS

If there is a penetrating wound of the neck, traumatic internal carotid artery thrombosis is more likely to be recognized, but if there is merely a

contusion with a minor degree of swelling and ecchymosis in the supraclavicular fossa this diagnosis may be overlooked. In patients who present clinical signs and symptoms simulating those of acute head injuries the diagnosis of thrombosis of the internal carotid artery may be suspected when a combination of neurologic signs and trauma to the neck are observed.

In the majority of cases of acute thrombosis of the internal carotid artery the signs and symptoms may develop within a period of 6 to 24 hours,[13] as contrasted to the longer interval for spontaneous thrombosis. The clinical manifestations of these lesions depend upon several factors: (1) the extent of the thrombosis, (2) the competency of circulation in the circle of Willis, (3) the presence of vasospasm, (4) the presence of the lesion in the dominant or minor hemisphere, (5) the severity of associated craniocerebral injury, (6) the degree of secondary hypoxia. These may result in alterations in the state of consciousness, hemiplegia, aphasia, blindness, visual field defects, and Horner's syndrome.[3,34]

If the patient is cooperative the measurement of the retinal artery pressure by Bailliart's ophthalmodynamometer may give a definite indication of the presence of this lesion.[1,5,31] Using this technique the first pulsation of the retinal artery as observed by funduscopic examination with pressure on the globe corresponds with the diastolic retinal pressure (35–40 mm.) and the last beat with the systolic pressure (70–75 mm.). In thrombosis of the internal carotid artery the diastolic and systolic pressures are reduced when compared to the normal eye. Since the accuracy depends upon the cooperation of the patient this procedure is of limited value in an agitated or irrational individual.

Caldwell and Hadden[2] have indicated that "absence of the temporal pulse on the involved side is good confirmatory evidence that the common carotid and possibly the external carotid artery is occluded." However, palpation of the vessels in the neck is of no value in diagnosis of the process in the internal carotid artery. In the occluded artery, pulsations may be transmitted to the thrombosed segment from the more patent portion.

The presence of increased intracranial pressure with thrombosis of the carotid artery is now well recognized. Caldwell and Hadden,[2] in their review of the literature on thrombosis secondary to penetrating wounds of the carotid artery, noted a definite elevation of cerebrospinal fluid pressure on lumbar puncture. Riechert[25] and Moniz *et al.*[20] observed papilledema in cases of spontaneous thrombosis of the carotid artery suggesting increased intracranial pressure. The development of unilateral cerebral edema was recognized in a shift of the ventricular system toward the contralateral side in 3 cases 3, 6 and 12 days after the onset of signs of thrombosis by Elvidge and Werner[9] with confirmation by Raney[24] and Caldwell and Hadden[2] in autopsy material. In spite of subtemporal decompression, this increased intracranial pressure may be so marked as to produce definite temporal and cerebellar pressure cones, as illustrated in Case 2.

Angiography presents the most accurate method of diagnosing throm-

bosis of the internal carotid artery during life. Johnson and Walker[13] have emphasized that if percutaneous arteriography is used the angiogram should be taken in such a fashion that the bifurcation of the common carotid artery is shown, so that one can observe the extent of filling of both the external and internal branches. We believe that it is also advisable to include the needle tip in the angiogram in the percutaneous method, in order to rule out faulty injection technique, such as injection into the external carotid artery or extra-arterial tissues. If the diagnosis of carotid thrombosis is reasonably certain it is better to use the open method of arteriography. This allows direct visualization of the internal carotid artery permitting more accurate injection, enables an estimate of the degree of injury to the vessel and surrounding tissues, and, if thrombosis is demonstrated, cervical sympathectomy may be done immediately.

Although bilateral angiography in these cases of occlusion of the carotid artery may demonstrate the collateral circulation through the anterior communicating and anterior cerebral arteries this appears to be definitely contraindicated in the traumatic group. The risk of such a procedure is recognized in spontaneous carotid artery thrombosis, and it is no doubt more dangerous in acute occlusion where the collateral circulation has probably been placed on a more acute strain.

The problem of the differential diagnosis between an expanding intracranial hematoma and internal carotid artery thrombosis may be a difficult one. If there is progressive impairment of the state of consciousness, or there are signs of a tentorial pressure cone or changes in the vital signs suggesting increased intracranial pressure, burr holes are indicated under local anesthesia to rule out the possibility of an acute subdural or extradural hematoma. If no pathological condition is found and the brain shows signs of being under increased pressure, a ventriculogram may disclose signs of unilateral hemispheric lesion. Angiography will permit differentiation between carotid artery thrombosis and an intracerebral lesion.

TREATMENT

Prompt diagnosis of arterial thrombosis with as little delay as possible in instituting treatment should be the goal of every surgeon. Constant observation of all patients with suspected arterial injury and immediate institution of therapy are factors of paramount importance to success in treatment of this lesion. If the diagnosis of thrombosis of the internal carotid artery can be made early by percutaneous arteriography, anticoagulant therapy may be of value in controlling the progression of the intravascular clot, but it will not affect the thrombosis that has already taken place. If the clotting of blood is progressive it will reduce the efficiency of collateral arterial circulation by actual extension into the collateral arteries. Treatment in these cases should be directed toward increasing the blood flow through the collateral channels, which involves overcoming the reflex vasoconstriction distal to the site of thrombosis. This may be attempted by continuous cervical sympa-

thetic blocks administered by inserting a polyethylene catheter into the region of the sympathetic chain as suggested by Poppen.[23] Cervical sympathectomy[29] is more permanent and probably more satisfactory. Papaverine as a supplementary vasodilator should be administered.

Because the thrombosed vessel is considered to cause a reflex spasm of the distal vessels, excision of the thrombosed vessel has been performed on several occasions.[14,15,20] In their review on spontaneous internal carotid artery thrombosis Johnson and Walker[13] stated that this procedure was used in 28 cases in the literature with improvement in 7 patients. However, they question the advisability of the procedure, for recanalization of the thrombosed carotid artery has been known to occur.

In those cases in which thrombosis has been extensive and signs of increased pressure and cerebral edema are present, early bilateral subtemporal decompression may be of some benefit in preventing pressure on the medullary and midbrain centers by prevention of cerebellar and temporal pressure cones. In the unconscious patient cerebral edema may be reduced by maintaining an adequate airway by intratracheal suction or tracheotomy.[6,30] Supplementary oxygen will afford a better chance of adequate oxygenation of cerebral tissue.

SUMMARY

Traumatic internal carotid artery thrombosis *secondary to nonpenetrating injuries to the neck* should be considered in the differential diagnosis of craniocerebral trauma. Five cases of concomitant head injury and traumatic internal carotid artery thrombosis of this type were found in the literature. These have been described and we have added 2 similar cases. The diagnosis and treatment of this lesion have been presented in detail.

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PHANTOM LIMB IN PARAPLEGIC PATIENTS

REPORT OF TWO CASES AND AN ANALYSIS OF ITS MECHANISM*

ALBERT W. COOK, M.D., AND WILLIAM H. DRUCKEMILLER, M.D.†

Department of Neurosurgery, State University of New York, College of Medicine at New York City, Brooklyn, New York, and United States Naval Hospital, St. Albans, Long Island, New York

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THE persistence of established knowledge concerning the body schema after removal of a part or all of an extremity has been termed the phantom limb syndrome. Adherence to this definition arbitrarily excludes from the present discussion those individuals with phantoms associated with lesions at various levels of the nervous system, but in whom there has not been an amputation. Also omitted from consideration are the so-called phantom limbs of some psychotic patients.

Mitchell[17,18] Leriche,[13] and Livingston[16] all recorded the presence of phantom limbs in over 90 per cent of all patients who had had an amputation. Pain is not a constant feature of this syndrome, as indicated in the report of Browder and Gallagher,[3] who found it to be present in approximately 30 per cent of their patients. Furthermore, only 20 per cent of this group of patients, or 6 per cent of their total series, experienced pain of an enduring character. In spite of the common occurrence of the phantom syndrome little attention had been directed to its pathophysiology until the introduction of various surgical procedures designed to relieve the associated pain. Among the first surgical endeavors aimed at the relief of pain were resection of neuromata of the neural stumps and division of peripheral nerves.[18] Subsequently, anterolateral[4,7,23] and posterior cordotomies,[2,3,20] sympathetic ganglionectomies,[23] and ablations of a part of the parietal cortex[6,9] were performed. Although some success was obtained with these procedures in certain instances, the results in general left much to be desired. The great difficulties encountered in dealing with this problem have been vividly illustrated by the report of Lhermitte and Puech.[14] In a period of 18 years a patient with pain in a phantom limb was not relieved by a resection of a neuroma, paravertebral novocain block of sympathetic nerves to the part, posterior myelotomy, and finally resection of a part of a parietal lobe. In the past few years Riddoch,[21] Stone,[22] and Henderson and Smyth[11] have attempted to establish the basic physiology of sensations of phantom limbs. The latter authors believed that the characteristics of a phantom part may be assigned to three levels of neural activity, namely "psychogenic, sensorimotor cortex,

* The patients considered in this study were from the United States Naval Hospital, St. Albans, Long Island, N.Y. The opinions of the authors expressed herewith do not necessarily represent those of the Bureau of Medicine and Surgery of the Navy Department or of the Naval Service at large.

† Assistant Attending Neurosurgeon, Kings County Hospital, Brooklyn, N.Y. Now stationed at the United States Naval Hospital, St. Albans, Long Island, N.Y.

and peripheral nerve." They introduced the term "natural phantom" to describe the persistence of a painless normal body pattern after amputation of a part, therefore setting apart this aspect of the problem from the various epiphenomena such as severe unrelenting spontaneous pain, distorted posture and involuntary spasmodic movements. The latter were considered to be related to "psychological" factors whereas the natural phantom was dependent on an intact sensorimotor cortex. More recently, Li and Elvidge[15] have chronicled observations on a phantom limb in a paraplegic patient. Multiple procedures directed at the lower levels of both the somatic and vegetative nervous systems were of no avail, finally, in assaying the pathways of afferent impulses from the ghost part or in changing its character. Bors,[1] also, has documented the existence of phantoms in paraplegic patients below the site of injury and has postulated a mechanism that requires further consideration.

It is because of the many and apparently contrary views related to certain aspects of phantom limbs as well as our interest in the pathophysiology of this phenomenon that the following examples of the phantom limb syndrome in paraplegic patients are presented.

CASE REPORTS

Case 1. E.G., a 24-year-old pharmacist mate in the United States Navy, was injured on Feb. 19, 1945 when a mortar shell exploded within 2 feet of him. Shrapnel entered his spinal canal at the levels of the 7th and 11th thoracic vertebrae, rendering him paraplegic.

Clinical examination at this time showed evidence of a complete physiologic interruption of the spinal cord at the 11th spinal cord segment. This level changed slightly during hospitalization in that the motor and sensory loss became absolute only in the lower extremity with recovery ensuing in the lower abdominal segments.

After recovery from the initial injuries he suffered from the usual sequelae associated with the paraplegic state, including paroxysmal spasm of the lower extremities. On May 7, 1948, both obturator nerves were crushed in an attempt to relieve these spasms. Since this did not entirely relieve the recurring contractions, part of the motor components of the cauda equina were divided on June 23, 1948. The anterior roots of lumbar nerves 2, 3, and 4 were sectioned under direct visualization at their point of emergence into the dural sleeves. The remainder of roots comprising the cauda equina were stimulated with a current of 5 volts and in those instances in which gross muscle contraction resulted, the stimulated root was sectioned. Thereafter, the lower extremities were flaccid and the spasms were abolished. On Nov. 8, 1949, a right mid-thigh amputation was performed because of persistence of a large infected decubitus ulcer of the knee.

On the first postoperative morning the patient first complained of a phantom limb. As with many patients with this syndrome he was, at first, unable to reconcile the objective absence of his limb with the fact that it felt as if it were still present. This conflict must have been particularly disturbing since he said, "This one (left lower extremity) is here and dead, but this one (amputated extremity) is gone, yet it feels alive." From his description there was apparently a distinct sensation of viability in the phantom, and, subsequently, he explained that it felt as if he could

kick someone with it. Both the ankle and the toes of the phantom were "cramped like the cramps of a Charley horse," and both of these parts were felt to be in a position of extreme plantar flexion even though the limb otherwise seemed to be of normal shape and size. This abnormal position of the toes and ankle was not painful, but a burning pain was present in the leg "like when your arm goes to sleep and you rub it." There was no pain in the knee. The sensation of a cramped posture of the phantom limb persisted intermittently and at times the entire phantom burned during stormy weather or when a storm seemed imminent. There had never been any jerking movements in the ghost and proximal displacement of the distal part of the phantom had never been recognized. Voluntary movement of the phantom had not been possible, but the limb seemed to change position with a change in posture of the intact lower extremity. When resting in bed the phantom would become less prominent and when seated in a wheel chair it seemed to be flexed. Even after the phantom had become less vivid he would maneuver his wheel chair away from objects for fear of bumping the phantom limb.

Comment. In this instance, as in Case 2, a fairly typical phantom appeared after amputation in spite of the physiologic interruption of the spinal cord and the anterior rhizotomy. It is noteworthy that involuntary positional changes were present and that voluntary movement of parts of the phantom was impossible.

Case 2. C.S., aged 31 years, sustained a gunshot wound in his back on May 22, 1946 with concomitant complete physiologic interruption of the spinal cord at the 7th thoracic spinal cord segment. On Aug. 6, 1946, a bilateral anterior rhizotomy of the 12th thoracic, and 1st, 2nd and 3rd lumbar roots was performed in an effort to reduce flexion spasms in the lower extremities. In Nov. 1947, the left lower extremity was amputated at mid-thigh for suppurative arthritis of the knee joint.

He was transferred to our hospital $1\frac{1}{2}$ years later, when information relative to his neurologic status and phantom was first obtained. The level of spinal cord interruption was essentially as recorded except that the level of absolute sensory loss had descended two to three segments. A phantom limb was perceived and there appeared to be no difference in it from that of the other extremity; they were both numb and asleep. The occasional burning that seemed to be in the ghost part was the same as the burning sensation he often experienced in the other leg. The size and shape of the phantom were similar to those of the intact extremity; however, the ankle and toes of the former seemed slightly prominent. There was the feeling that the phantom moved when the position of the other extremity was changed. On Jan. 5, 1949, a second rhizotomy was performed because of continued muscular spasms in the stump of the left thigh and in the right lower extremity. The roots comprising the cauda equina below what was presumed to be the 2nd lumbar root were stimulated with a current of 5 volts and in the instances in which gross muscle contraction ensued, the stimulated root was divided. This procedure did not alter the phantom in any way.

Comment. This patient was reluctant to discuss the matter of a ghost limb and possibly some of his answers lacked accuracy. Yet, he seemed well aware of a phantom and that movement of the ghost part was impossible even though involuntary movements of the stump of the left thigh and the right lower extremity did occur.

MECHANISM OF PHANTOMS

The relationship of our deductions to previously stated views on the subject may be best evaluated after restating some of these existing ideas. Riddoch[21] visualized the mechanism of the production of the phantom limb as being due to projection of sensory impulses from the proximal ends of the divided peripheral nerves in the stump. He believed that impulses originating from this peripheral source acted to maintain the integrity of the body schema and in terms of the schema were "interpreted as if the limbs were still present." Livingston[16] was in accord with these thoughts but added, "There must be a third agency interposed between the peripheral sources of irritation and the plastic model of self. It is a physiologic agency that I think exists as being the spinal cord, on which the original irritants act to bring about the abnormal state of blood vessels and sweat glands, the cutaneous hyperesthesia and the changes involving the skeletal muscles. In my opinion the internuncial pool may be the agency which acquires a momemtum that may obviate a cure by reamputation or excision of neuromata."

Gillis[8] believed that phantom limbs appeared because of disruption of the normal stream of impulses to the cortex from the peripheral neuromuscular structures. "It is the readjustment of the remaining muscles of the body to the altered state which now throws additional strain on the sensitized cerebrum and makes the previously existing state of equilibrium so labile to upset. It is the constant effort of the central activity to maintain this equilibrium between the continuous stream of impulses from the remaining part of the body which makes a phantom limb an ever present possibility and brings the awareness of the absent member to consciousness."

Henderson and Smyth[11] also suggested that the "natural phantom" depended upon changes in the spontaneous activity threshold in the cortex following the loss of those impulses it normally receives from the amputated part. They further stated that "the complete absence of impulses from a limb after spinal transection may account for the absence of a phantom in spinal lesions." In their study of some 300 cases of amputation they had never encountered a true phantom after complete physiological interruption of the spinal cord. Subsequently however, and as noted previously, Bors[1] and Li and Elvidge[15] presented evidence to the contrary. Still Henderson and Smyth did propose that the natural phantom was dependent upon the sensorimotor cortex. Browder and Gallagher,[3] also, indicated that it was the basic sensorimotor pattern in the cerebral cortex that was responsible for the appearance of phantoms. In consideration of these, in part, conflicting concepts the problem of phantom sensations in patients with complete physiologic interruption of the spinal cord assumes particular significance.

The mere existence of phantom limb in patients with complete physiologic interruption of the spinal cord is evidence that is contrary to the ideas that this phenomenon is due to the projection of impulses from peripheral nerve stumps. The view that such impulses must traverse the spinal cord on their course to the sensory cortex also becomes untenable. Although the

notion of Gillis regarding disruption of normal sensory impulses to the sensory cortex may be partly correct, such a disturbance must have a greater scope than simply that of the proximal and distal limb muscles as proposed by Henderson and Smyth, since in our patients the entire limb lacked continuity of somatic nerves.

Bors' ideas also, can not be reconciled with existing data. His theory of cross-stimulation at the site of damage in the spinal cord (paraplegic phantoms) and at the point of division of peripheral nerve (amputee phantoms) presupposes that stimuli traverse this "artificial synapse" and "initiate reverberating circuits from the damaged region" ultimately to reach "cortical levels." Such a mechanism for both types of phantom (paraplegic and amputee) may seem adequate, granting the existence of the artificial synapse, but when spinal cord interruption is superimposed upon an amputee phantom or vice versa such a mechanism can not be accepted in view of existing facts. Specifically, the pathway for mediation of impulses to the cerebrum from the artificial synapse has been interrupted. In general, then, some mechanism other than the proposed peripheral alterations must be postulated to explain the existence of phantoms.

ASSOCIATED PHENOMENA

In addition to the presence of a phantom in patients who have had amputations of a part or all of an extremity, there are two other interesting phenomena often associated with this state; namely, movement (voluntary) of parts of the phantom and so-called automatic movements (involuntary).

The voluntary movements of parts of the phantom are essentially some of the movements that could be normally performed before the amputation of the part. However, they are usually restricted in that possibly only flexion or extension may be executed at a joint and furthermore either one of these movements may be weaker than the other. When the phantom becomes less prominent such movements are more difficult to perform. Associated with such movements there may be contraction of appropriate muscles in the stump but following denervation of the musculature of the stump such movements disappear. The absence, then, of the ability to perform such movements in our patients is readily understood since not only were the muscles of the stump peripherally denervated by rhizotomies but the long cerebrospinal pathways had been physiologically interrupted. Automatic knee movements were, however, present in both patients. When they were sitting in a wheel chair the phantom leg would flex and when supine in bed it would extend, assuming the posture of the intact extremity. These movements of the ghost part could not be voluntarily executed or stopped. Henderson and Smyth recorded similar observations and suggested that they reflected the normal more automatic control of the postural muscles in a limb. It was their belief also that such movements "may be mediated through reflexes at a lower level in the nervous system than those concerned with the sensory phantom and its voluntary movements." Yet in our patients, in addition to

a lesion interrupting the spinal cord pathways, the reflex arc of the lower extremities had been interrupted by the division of the anterior roots of the cauda equina; still, movements of the phantom were present.

AUTHORS' CONCEPT

Although information such as has been presented seems to lend some understanding to phenomena associated with phantoms a satisfactory explanation of the entire syndrome and its subtending mechanisms still cannot be formulated completely. With due regard to the danger of anatomizing abstractions, a recapitulation of certain of the more relevant issues does permit resolution of part of the problem.

Head and Holmes[10] established the basis of the concept of the body schema when they referred to the plastic model in which every new posture or movement was recorded and how the activity of the cerebral cortex brought into proper relationship every fresh group of sensations evoked by altered posture. However, the experience and memory of such sensory events were given no significance. Hughlings Jackson[12] stated the problem of memory simply when he said, "There is no faculty of memory apart from the things remembered." Such memory is derived from sensory impressions, sometimes necessary of repetition, and is nourished by the ability to synthesize such events into an integrate whole. From birth, visual, auditory, proprioceptive, and tactile impressions are recorded and ultimately constitute "things remembered" or our memory. A congenitally deaf child has no auditory memory or if blind, no visual memory. Contrawise, if the perceptual apparatus functions normally and the image be defective as compared to other normals, then the memory of such, as a defect, will not exist unless it is so demonstrated subsequently. Patients with congenital disturbances of the distal spinal cord are excellent examples illustrating this fact. These people can be shown to have areas of altered sensibility of which they were unaware up to the time of its delineation by physical examination following which the abnormal zone persists distinctly. Browder and Gallagher[3] demonstrated indirectly this fundamental process with particular relation to phantoms when they observed that a ghost part was not present in individuals born without one or more limbs or in whom an amputation had been done prior to the third year of life.

Observations such as these do not entirely preclude the participation of the lower levels of the nervous system in the maintenance of the body pattern under normal circumstances, but rather emphasize the importance of other factors, the major one being sensory experiences.

Head and Holmes, Gillis, Henderson and Smyth, and Cronholm[5] alluded to the possibility of heightened activity of the cerebral cortex in patients with ghost parts but did not pursue the thought. Extension of this idea and correlation of our formulations regarding memory seem possible in view of the recently reported experiences of Penfield and Rasmussen[19] with the human cerebral cortex. According to these authors, epileptic discharges from

the sensorimotor cortex produce elementary response patterns whereas areas immediately anterior or posterior to the sensorimotor strip are required for elaboration of a phenomenon. "The supposition is, therefore, that there is a frontal and a parietal field for the elaboration of acts." Acquired neuronal patterns were considered to be related to temporal lobe activity. In the temporal cortex "the stimulating electrode may present to consciousness vivid memories, auditory memories or combined memories. The elements of memory may come from actual experience, from the individual's reading, or from his dreaming. Apparently the memory that is stored or 'filed' in the temporal cortex, whether visual picture, musical piece or significant experience must have come to the patient's attention before being filed there. The thousands of visual impulses that reach the occipital cortex and serve to guide a man in his daily task but which he does not 'notice' do not seem to find any lasting repository in the temporal cortex.

The things he can remember, the thing on which he has focused his mind, these are things which may become the substance of his minor seizures or the product of electrical stimulation."

It seems, then, that the appearance of a phantom following amputation of a part or all of a limb is in many respects comparable to phenomena associated with heightened activity of the temporal (memory) cortex and less intimately associated with known function of the sensorimotor elaboration areas. The memory of previous experiences is recalled and things on which one has his attention are pre-eminent. The digits, hands and feet are the prominent parts of the phantom and are certainly parts on which one "focuses" his attention. The small or large hand of the phantom seems somewhat comparable to the perceptual illusions of large (macropsia) or small objects (micropsia) or the so-called Lilliputian hallucinations associated with temporal cortex discharge. In addition, the individual experiencing the phantom is faced with the conflict of a real and unreal part as the patient with temporal lobe seizures has feelings of unreality amidst the actual realization of circumstances. The parallelism of these two phenomena, that of temporal lobe seizures and some of the characteristics of the phantom limb, is striking and allows the speculation that the phantom represents a memory established after prolonged sensory experience of a part and that its appearance is dependent upon a functioning cerebral cortex, primarily postrolandic in position, and encompassing the temporal area. This designation is not to be construed to signify that memories of the phantom or images of an amputated part are "stored" or "filed" in one particular part of the brain. Its purpose clearly is to abrogate such previous considerations of gnostic centers and to emphasize the participation of a widespread neural network encompassing a heretofore neglected system; namely that concerned with memory and temporal lobe function.

SUMMARY AND CONCLUSIONS

The term phantom limb is defined as it applies to this report. A brief account of the development of the more recent concepts of this syndrome is

given. Two cases of the phantom limb syndrome in patients with complete physiologic interruption of the spinal cord are reported. An interpretation of this syndrome is presented based on the observations of these cases.

As a result of this analysis the following conclusions seem warranted:

1. That the natural phantom limb, as defined by Henderson and Smyth, is not dependent on stimuli arising in the peripheral nerve stump or other structures of the remaining stump.

2. That some of the associated phenomena present in this symptom complex are dependent upon the normal function of, at least, part of the spinal cord and peripheral neuromuscular structures.

3. That the ability of the human brain to recall the memory of the body schema is a primary factor in the phantom limb syndrome.

4. That a consideration of known physiology of the human temporal cortex suggests that the presence of a phantom limb is intimately associated not only with previously considered gnostic (parietal) areas but also must find some dependence on neural networks within the temporal area.

5. That the pathophysiologic correlations presented indicate a need for reorientation and re-evaluation of our present methods of management of the phantom limb problem.

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THE OCULAR COMPLICATIONS OF CAROTID ANGIOGRAPHY

THE OCULAR SIGNS OF THROMBOSIS OF THE INTERNAL CAROTID ARTERY*

FRANK B. WALSH, M.D., AND GEORGE W. SMITH, M.D.
Wilmer Institute of the Johns Hopkins Hospital and University, and The University Hospital, Baltimore, Maryland

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CEREBRAL angiography often is essential to the diagnosis of thrombosis of the internal carotid artery. The ocular symptomatology that may be associated with such angiography is described without the benefit of statistics in Part I of this paper.

Since cerebral angiography has become widely utilized thrombosis of the internal carotid artery has become a generally well known clinical entity. In 1951 Johnson and Walker[10] in describing the angiographic diagnosis produced a table of symptomatology which included the ocular signs in 107 verified cases. Part II of this paper concerns the ocular signs of thrombosis of the internal carotid artery.

PART I. CEREBRAL ANGIOGRAPHY—OCULAR SIGNS

Angiography of the Ophthalmic Artery

Up to the present angiography of the ophthalmic artery has had relatively little value in the diagnosis of arterial obstructions. The artery is not constantly visualized when presumably it is functioning normally; within the cranium it is relatively fixed in position; its course in the orbit is variable and abnormalities are difficult to assess; the branches of the artery are small, and although in some instances they may be identified with reasonable certainty, such recognition has little practical value. In our material the ophthalmic artery can be identified in at least half the films taken within 2 seconds after the injection of diodrast.

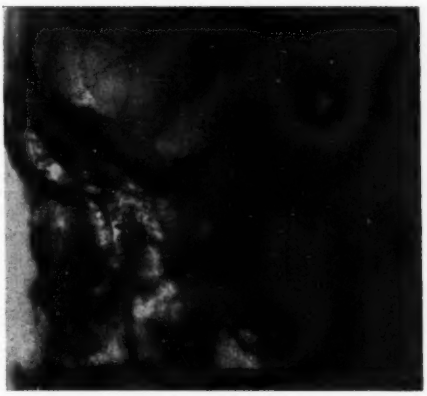

FIG. 1. Lateral angiogram taken at 5½ sec. showing choroidal plexus and ophthalmic artery (Schurr).

Schurr[16] has described what may ultimately prove to be an important angiographic finding. In lateral angio-

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grams (Fig. 1) taken about 5½ seconds after injection there is seen to develop a thin crescent of opacity in the outer two-thirds of the orbit. This crescent forms from above downward just as the ophthalmic artery is fading out. According to Schurr the curved opacity represents filling of venous channels (the choroidal plexus) within the eye.

Ecker's textbook[6] contains many arteriograms showing the ophthalmic artery.

Symptomatology Associated with Angiography

Pain. In many cases at the moment diodrast is injected into the common carotid artery a burning sensation, often described as painful, occurs in the homolateral side of the face. Usually in this area there is some degree of flushing and this may be preceded by short-lived pallor. The abnormal sensations in the face are associated with filling of the external carotid system, as might be anticipated from the arterial distribution. Such sensations have been present in individuals whose internal carotid artery was thrombosed.

Pain in and about the eye is described in many instances. This complaint comforts the surgeon because it indicates that the contrast medium has entered the internal carotid artery. Doubtless, such pain may develop occasionally when the internal carotid artery is thrombosed because there is a liberal collateral circulation from the external carotid system to the ophthalmic artery.

In a single case there was complaint of a sensation of a foreign body in the eye only during and for a few moments after each of 6 injections.

In some instances there is complaint of burning pain in the face and behind the eye as well, but rather often one complaint overshadows the other. Almost invariably in such cases both internal and external carotid systems have filled.

The mechanism underlying these symptoms and signs is not known with certainty. In all probability the contrast medium excites spasm of the vessels which are filled and the resultant irritation of sensory nerves in the vessel walls produces pain.

Retinal Irritation. According to Schurr[16] the patient often describes a flash of light as the injection is being made. He has attributed this symptom, with which we have no experience, to retinal irritation.

Pupillary Changes. Changes may be observed in the pupil of the homolateral eye in a minority of cases. Dilatation of the pupil occurs as the injection is being made in possibly 25 per cent of cases. Usually the dilatation is of brief duration, a matter of seconds or minutes, but in occasional instances it may persist for hours. Narrowing of the pupil is said to have been observed in a case with which we are familiar, as also has momentary hippus.

The mechanism responsible for pupillary changes is not known. Possibly stimulation of sympathetic fibers is responsible for the dilatation but at what level would be mere conjecture.

Retinal Vessels. According to Schurr[16] and others there is momentary narrowing of the retinal vessels during angiography. This narrowing is said to

be followed by widening. Such changes cannot be identified with the ophthalmoscope in many instances and we have not observed them. It would be anticipated that with any visible narrowing of the retinal vessels there would be an associated blurring of vision and this is notable by its absence in a vast majority of cases.

Hemorrhages in the Skin, Conjunctiva and Retina. Following the injection of thorotrast or diodrast petechial hemorrhages have been observed in the skin of the face and about the eye homolateral to the injection, in the conjunctiva, particularly in the lower fornix, and in the retina. Falls, Bassett and Lamberts[7] studied 80 consecutive arteriographies to determine ocular complications. They found that petechial hemorrhages could be visualized in some instances on completion of the injection and in others in from 30 to 90 minutes after the injection had been made. Considering all ocular complications they found that one or more occurred in 86.3 per cent of their cases. Petechial hemorrhages occurred in the skin in 43.8 per cent; in the conjunctiva in 81.3 per cent; in the retina in 25 per cent. The retinal hemorrhages were round, granular and occasionally preretinal and occurred usually in the posterior pole. They also described cotton-wool exudates as present in some instances. Our observations suggest that the percentage figures given by Falls *et al.* are on the high side, but we have not examined meticulously a similar consecutive group of patients subjected to angiography. We have not yet observed cotton-wool exudates. Petechial hemorrhages in the skin and conjunctiva have disappeared in our experience within a few days or a week at most.

Allergy? to the Contrast Medium. In some cases the injection of small amounts of contrast medium produces alarming symptoms.

Case 1. A 46-year-old colored female (V.P.U.H. 57484) was admitted complaining of severe headache of 4 days' duration. There was severe pain in the left side of the head and about the left eye, shifting to the occiput.

B.P. 170/100, pulse 60, respirations 18. Babinski's sign was present on the right. CSF pressure was 540 mm. of fluid. The fluid contained many red blood cells.

After several days in hospital a left carotid arteriogram was agreed upon. Under local anesthesia 3 cc. of 35 per cent diodrast were injected into the common carotid artery. There was an immediate onset of aphasia and right hemiparesis. No further diodrast was used. Three and a half hours later small petechial hemorrhages were apparent over the entire left side of the face, head, and neck above the level of the needle puncture; the hemorrhages stopped at the exact midline of the face. Petechial hemorrhages were present in the conjunctiva but if any were present in the retina they were overlooked. Five days later the petechial hemorrhages had almost completely disappeared. The aphasia and hemiparesis disappeared within 24 hours after their development. Then a normal arteriogram was obtained using 8 cc. thorotrast without reaction. Subsequently a further test was performed using 3 cc. of diodrast 35 per cent and again there was development of hemiparesis and aphasia but there were no superficial petechial hemorrhages.

It has been suggested that sensitivity to diodrast or other contrast media may be predicated on the basis of the response to instillation of a drop of

the substance into the conjunctival sac. We do not have sufficient experience to have an opinion regarding the value of such a maneuver. In all cases 1–3 cc. of a 1:1000 solution of diodrast should be injected intravenously preliminary to arteriography. If untoward symptoms arise during the injection no further diodrast should be injected.

Changes in Visual Acuity. There has been a remarkable infrequency of changes in visual acuity in individuals subjected to angiography in the sources of our material—The Johns Hopkins, Baltimore City, University and Mercy Hospitals—where approximately 1200 angiograms have been made. Actually there have been only 2 such cases in our series, and these are summarized below (Cases 3 and 4). Falls, Bassett and Lamberts[7] have noted a much higher incidence of visual loss. In 80 consecutive arteriographies they observed temporary loss of vision (10 to 30 minutes) in 2 cases and "severe optic neuritis" in 1 patient with eventual complete loss of vision. Tarlov and Rosenberg[21] observed homolateral occlusion of the central retinal artery immediately after the injection of diodrast. They suggested this occurrence may have been caused by failure to maintain a flow of saline between injections of diodrast. Our Case 3 is similar to the following case reported by Curtis.[5]

Case 2 (Curtis' case). "Male, aged 67 years. Two years before admission this patient had suffered from coronary thrombosis, and three months before admission he complained of the sudden onset of 'pins and needles' in his left hand, followed by persistent weakness and clumsiness. Subsequently he had several more attacks of 'pins and needles,' each lasting a few minutes. There was present a left lower facial weakness and weakness of the left thumb and index fingers, with a considerable cortical sensory loss in the left hand. Blood pressure was 170/95 mm. Hg., and the peripheral vessels showed moderate thickening.

"On May 18, 1949 right percutaneous carotid puncture was carried out. Following one injection of 12 cc. of 35 per cent pyelosil he developed a focal fit involving the left arm and leg. There was a transitory loss of consciousness followed by stupor. No more injections were made and he was given phenobarbitone (3 gr.) intramuscularly. Later in the day he complained of poor vision in the right eye, but next day he had improved. On May 20 the ophthalmologist diagnosed a spasm of the right retinal artery and antispasmodic treatment was begun. Some recovery of vision took place, but on discharge from hospital on June 6 there was still a central scotoma of that eye."

Case 3. I.V.F. (591170), a 60-year-old white man, in 1940 had a left facial palsy and changes in sensation over the left half of the body. There was severe headache during a single day. Recovery followed within a few weeks. In May 1949 he experienced difficulty in manipulating the fingers of the left hand for 2 days. In June 1949, during 2 days, paresis of the left arm and leg developed. Within 2 weeks he could walk with a cane. In October 1951 there developed difficulty with his speech and this persisted for 5 days during which time he was unsteady in walking and felt generally "miserable." Recovery followed within a few days.

On Nov. 26, 1951 a right carotid arteriogram was made. The internal carotid artery did not fill but the external carotid system filled well. During the procedure he described burning of the right side of the face. Four hours after the arteriogram

was obtained he awakened from a nap and found the vision in the right eye was reduced to hand movements. Vision in the left eye remained normal. There was said to be some edema of the macula visible with the ophthalmoscope but the retinal vessels were thought to be of normal caliber. A stellate ganglion block with novocain was done within 2 hours after the loss of vision had been reported, and this procedure was repeated 4 hours later. At the time of this second block the vision was improved. On the following morning when one of us saw the patient the visual acuity of both eyes was 20/20 and the fundi appeared normal.

Comment. The two cases cited above are similar as regards the onset of loss of vision. In both instances there was an interval of hours between the injection of the contrast medium and the loss of vision. It is possible that in both instances the injection of diodrast had nothing whatsoever to do with the episode of loss of vision. Two reasonable explanations for the visual loss are (a) retinal arterial spasm; (b) lodgement of an embolus. Curtis believed that the loss of vision in his patient was due to spasm of the central retinal artery and ophthalmoscopic examination of his patient at one time revealed pronounced narrowing of the retinal vessels. It would seem almost equally reasonable that recovery in his case followed the passing forward of a small embolus. In our case there is even less to offer in the way of an explanation for the transient blindness. The episodes of blindness are not proven to have been dependent on the injection of the contrast medium into the carotid.

We have observed a complication of angiography that has not been reported previously so far as we are aware: immediate loss of vision which arose as a result of the development of bilateral homonymous hemianopsia. This complication may have been dependent upon an elective variation in the ordinary technique of carotid angiography. In order to obtain bilateral filling of the internal carotid systems for purposes of direct comparison, when diodrast was being injected into the right carotid artery the left artery was digitally compressed.

Case 4. A 24-year-old woman. Severe headaches for 4 weeks, also several episodes of "black-out." Minimal weakness right arm; increased reflexes on right. Low-grade papilledema. Left carotid arteriogram obtained without incident; posterior cerebral artery filled. Right carotid arteriography with digital pressure on left artery to obtain direct comparison; normal bilateral filling including both posterior cerebrals. Onset bilateral blindness within seconds or at most a minute. Recovery light perception after stellate blocks made within 20 minutes. Ten hours later improvement in right homonymous half-fields. Next day right fields normal and 36 hours after onset both fields full and visual acuity normal for each eye.

E.M.M. (B.C H. 158215), a colored female aged 24 years, had suffered from occasional headaches for many years. For the last 4 weeks she complained of almost constant headaches. She described several episodes of "blacking out" when she became confused for a few minutes.

Examination revealed little of significance except for slight weakness of the right arm and increased reflexes on the right. B.P. was normal (118/70). Laboratory tests including serologic tests for syphilis gave normal findings. CSF pressure was 300 mm. fluid; cell count normal; Pandy reaction negative.

The eyes were normal externally. Visual acuity was 20/20 for each eye. There

was low-grade papilledema (less than 1 D.) in the right eye and more pronounced papilledema in the left eye (about 1 D.) The retinal vessels were said to be within normal limits although possibly a trifle narrow.

X-rays of the skull were read as normal.

With local anesthesia left carotid arteriography was done by percutaneous puncture. The arteriogram revealed normal filling; the posterior cerebral artery was filled. It was decided that a right arteriogram should be made. In order to fill both sides simultaneously pressure was applied over the left carotid artery as diodrast was injected into the right carotid. Within seconds or at most within a minute after this was accomplished there was development of total bilateral blindness.

With the onset of blindness the pupils became semidilated and responded sluggishly to light. The retinal arteries were said to have become narrowed but the discs and the retinae did not become pale.

Within 20 minutes after blindness developed a stellate block was done on each side and within a few minutes there was return of bare perception of light.

Within a few hours a postparietal trephine opening was made on each side and it was seen that there was much fluid on the left side. The left side only was needled and that with negative results.

Ten hours after the onset of blindness the patient described a sensation of grayness in the right homonymous half-fields. Within a further 14 hours there was return of function in these half-fields. In a further 24 hours the visual fields of both eyes were full and the visual acuity had reached normal levels in both eyes.

A pneumoencephalogram was performed which was read as normal.

Thirty-six hours after the loss of vision we examined the patient. The visual fields were full on confrontation test. The edema of the discs was as before noted. All the retinal vessels appeared a trifle narrow but otherwise the fundi were normal. Visual acuity was reported as, and seemed, normal.

The diagnosis was serous meningitis.

Comment. Case 4 is important for reasons which are obvious and are now briefly commented upon.

(1) It suggests that bilateral filling of the internal carotid systems obtained by such a maneuver as was used is a potentially dangerous procedure.

(2) That blindness in such a case should have developed on the basis of bilateral homonymous hemianopsia rather than as a result of interference with the blood supply to the retina of each eye seems worthy of notice. From the evidence at hand it seems apparent temporary interference with blood supply to the visual pathways occurred above the level of the geniculate bodies and pregeniculate gray matter. Seemingly the retinae were not rendered ischemic. The probable explanation is that the liberal collateral circulation from the external carotid system to the ophthalmic artery of each side provided sufficient blood to the retinae.

It may be further pointed out that "needling" as performed in this case does not ruin the argument for bilateral hemianopsia since it was performed on the left only and the right half-fields returned to normalcy before the left. Finally, the case is of interest because both posterior cerebral arteries filled. On the basis of the blood supply to the visual pathways, which will be con-

mented upon subsequently, it might be anticipated that in this case the posterior cerebral arteries arose directly from the internal carotid artery of each side.

(3) This case report and the two that precede it in this paper support Falls *et al.*: "The cause of these complications is not known, but they undoubtedly result from vascular change secondary to allergic, toxic or physical phenomena."

PART II. THE OCULAR SYMPTOMATOLOGY OF THROMBOSIS OF THE INTERNAL CAROTID ARTERY

Many cases are characterized by ocular signs: blindness of the homolateral eye; retinal hemorrhages; pain in the eye; hemianopsia; pupillary changes; ophthalmoplegia; papilledema.

The Arterial Supply to the Visual Pathways

Loss of vision and loss of visual fields are caused entirely, or in greatest part, by interference with the arterial blood supply; venous outflow probably is of minimal importance. In order to elucidate in some degree what interference with the arterial supply may produce in these cases, we have had prepared a diagrammatic representation of the arterial supply to the visual pathways (Fig. 2). This diagram has been drawn after study of the contributions of Beevor,[2] Abbie,[1] Wolff,[25] Brouwer and Zeeman,[3] Le Gros Clark,[4] and Shellshear,[17] and Lyle's[13] excellent photographs of specimens as well as injected specimens prepared in the University Hospital (G.W.S.).

Since the intraorbital portion of the optic nerve receives its blood supply from the ophthalmic artery exclusively it may be predicted with certainty that if this artery is sufficiently thrombosed to include the central retinal artery, blindness must result. All other structures comprising the visual pathways receive blood from more than a single artery. It seems probable that such a multiple supply would provide some degree of protection, and this may well be so. Furthermore, it would seem likely that structures containing cell centers (the retina, geniculate body, visual cortex) would suffer more profound damage from ischemia than would transmitting structures (optic nerve, chiasm, tract, and radiation). Our study of the arterial supply to the visual pathways as applied to clinical cases has added a single important conclusion based on anatomy: homonymous hemianopsia when it is a residual finding tends to be characteristic in that there is a tendency toward sparing of the upper quadrant of the abnormal half-fields.

To understand this feature of the hemianopsia attention must be directed to the arterial supply of the tract, the lateral geniculate body, optic radiation and visual cortex. The optic tract is supplied principally by the anterior choroidal artery. The lateral geniculate body receives its important arterial blood supply from the anterior choroidal and posterior choroidal arteries. The lateral portion of the nucleus receives retinal fibers from the inferior

homonymous quadrants of the retina. Obstruction of the anterior choroidal artery produces degeneration of the lateral aspects of the lateral geniculate body with consequent loss of the upper homonymous quadrants of the visual fields (Abbie[1]; Steegmann and Roberts[18]; Mackenzie, Meighan and Pol-

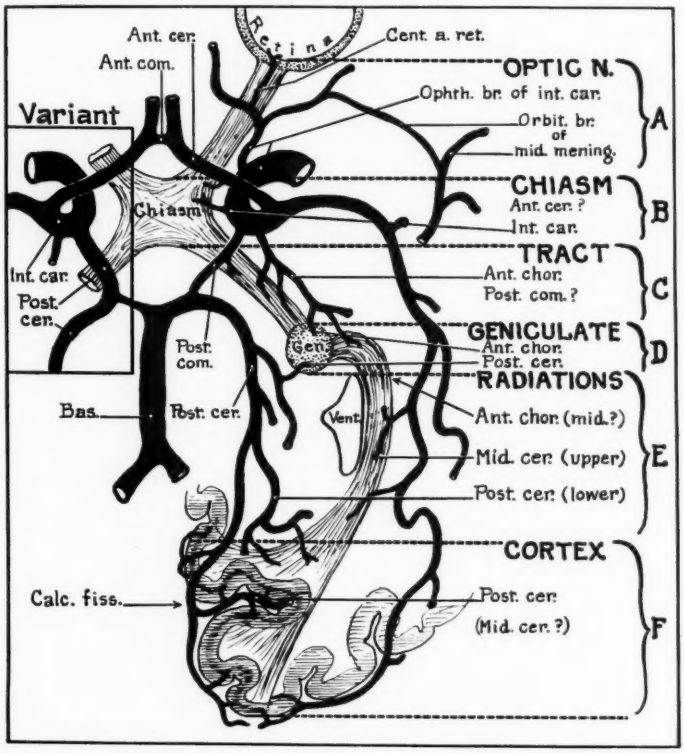


FIG. 2. Only principal arteries are shown in the diagram. Except for the intraorbital portion of the optic nerve all parts of the visual pathways have a multiple blood supply. There is great individual variation. The chiasm and tract have a more complicated supply than is shown (see Abbie[1]). The optic radiation in its anterior and middle portions receives blood from the anterior choroidal, and middle and posterior cerebral arteries but the relative extent of the supply from each of these arteries requires clarification. An anomalous origin of the left posterior cerebral is shown on the left side of the diagram. Such an arrangement occurs frequently but, by deduction, was not present in the cases of hemianopsia described in this paper. Further studies regarding the vascular supply to the visual pathways are being made by the authors.

lock[14]). An isolated obstruction of the posterior choroidal artery would result in the loss of the contralateral lower homonymous half-fields. Beevor's studies showed that the optic radiation in its anterior portion receives arterial blood from the middle cerebral (deep optic branch—Abbie), anterior choroidal and posterior cerebral with the upper two-thirds at this level receiving blood from the middle cerebral. The visual cortex as shown by Shellshear receives

a very major part of its supply from the posterior cerebral artery. With these considerations in mind it would seem probable that the characteristic hemianopsia, which is described and commented upon subsequently, indicates obstruction of the middle cerebral artery as a principal involvement.

Homolateral Blindness

Before cerebral angiography was utilized the diagnosis of thrombosis of the carotid artery was based on blindness or near-blindness of the homolateral eye and contralateral hemiplegia more pronounced in the arm than in the leg, also contralateral hemianesthesia. It was our experience that optic atrophy had become obvious by the time the patient appeared for examination. We now know that homolateral blindness occurs less often than contralateral hemianopsia, and that in a majority of recorded proven cases (65 of 107—Johnson and Walker[10]) there is no recognized ocular symptomatology. It seems likely that ocular signs may have been overlooked in some instances.

Often the loss of vision is preceded by transient attacks of blindness of varying severity which may recur during weeks or months. Such episodes often but by no means always presage permanent visual loss. When obscurations of vision precede blindness the permanent defect usually develops within a day or two. Monocular loss of vision may be recurrent and precede the development of hemiplegia and thereafter the eye may continue to function normally.

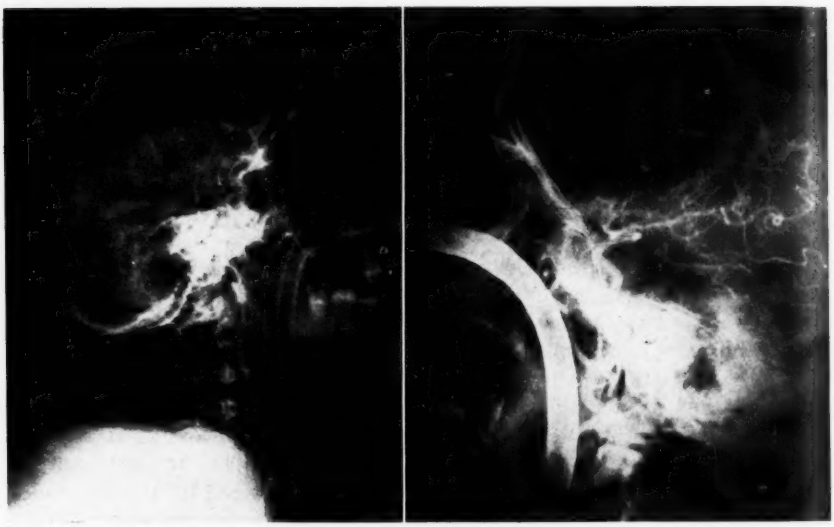
Fisher[8] has written an instructive paper regarding transient monocular blindness. He included 6 case histories illustrating such loss of vision as a manifestation of occlusion of the cervical portion of the internal carotid artery. The clinical course in his cases was characterized by brief episodes of monocular blindness followed after weeks or months by contralateral hemiplegia and cessation of the episodes of blindness. He emphasized the seemingly beneficial influence of the development of hemiplegia on the function of the eye homolateral to the internal carotid thrombosis. This has been our experience in 2 cases. It would seem that sparing of the affected eye might be due to increased collateral circulation from the external carotid artery, both homolateral and contralateral, following the development of the hemiplegia. Fisher's paper contains much that is instructive regarding monocular blindness not associated with thrombosis of the carotid artery. It would seem unnecessary, if not unwise, to consider what Fisher has described as a new syndrome; it is part of thrombosis of the internal carotid artery in which in some instances there is total absence of visual symptoms. It is conceivable that homolateral blindness, either permanent or temporary, may be the only symptom.

Undoubtedly in some cases of thrombosis of the carotid recurrent episodes of blindness of the homolateral eye occur over long periods after hemiplegia has developed. We have not observed this but colleagues have told us of 2 such cases.

In 1 case in which the diagnosis was established beyond question tem-

porary episodes of blindness occurred in the affected eye. The degree of visual loss and the visual field defects varied widely on different occasions. At one time there might be loss of upper field and in another episode loss of lower field or loss of a single quadrant or of central field. During such episodes the ophthalmoscope revealed retinal arterial narrowing in some instances affecting all the retinal arteries.

When homolateral blindness is a result of thrombosis of the internal carotid artery the obvious explanation is that the thrombus has extended along



FIGS. 3 and 4. *Case 12.* (*Left*) Left carotid arteriogram showing absence of filling of the internal system beyond the carotid syphon (the point of proven thrombosis). (*Right*) Right carotid arteriogram There is filling of both anterior and middle cerebral arteries.

the ophthalmic artery to the central retinal artery. In this regard it is of interest that the ophthalmic artery alone supplies blood to the intraorbital portion of the optic nerve. In cases of homolateral blindness the fundus picture is essentially that of closure of the central retinal artery. When there is absence of homolateral loss of vision we cannot state that the ophthalmic artery is not thrombosed but can only say that it is not extensively affected. If the artery is thrombosed close to the carotid the liberal collateral circulation from the external carotid branches of the same and opposite sides serves to maintain adequate blood supply to the eye. This is based on the fact that ligation of the ophthalmic artery close to the carotid does not result in blindness of the eye, and on experimental demonstration of free collateral circulation between the external carotid system and the ophthalmic artery in cadavers as originally done by Elschnig and later repeated and a-

plified by Walsh and King.[23] From a study of angiography in cases of carotid thrombosis the nature of this liberal collateral circulation is further verified. In Figs. 3 and 4 there was thrombosis of the internal carotid as determined by angiography and the site of the thrombosis was recognized at autopsy. Injection of the common carotid artery on the right provided filling of the left anterior and middle cerebral arteries and the patient was not blind in the left eye.

Atrophy of the optic nerve in rare instances may be incomplete as in Case 2 described by Sugar, Webster and Gurdjian.[20] As these observers have stated it is unlikely that in such cases there is any considerable involvement of the central retinal artery. Doubtless the small arteries that supply nutrition to the optic nerve are obstructed (branches from the ophthalmic, carotid, anterior cerebral).

It would seem reasonable to anticipate blindness of the homolateral eye as a common occurrence when both internal and external carotid arteries are thrombosed. Gurdjian and Webster[9] described homolateral loss of vision in 2 of 3 such cases; we have had 1 such case in which there was absence of visual symptomatology at all times (A.S., B.C.H. 109758)

Retinal Hemorrhages

We have identified retinal hemorrhages in only a single case (J.R., 458179—Case 2 of Johnson and Walker[10]).

It is remarkable that hemorrhages have not been observed more frequently when there has been temporary or permanent monocular blindness. Hemorrhages are not uncommon in cases of obstruction of the central retinal artery from whatever cause. In such cases they are venous in origin. There is included in Johnson and Walker's table a single example of obstruction to the central retinal vein on the side of the thrombosis. Such venous obstruction may be associated with arterial obstruction as may be seen in a specimen in the Wilmer Institute of Pathology Laboratory.

Homolateral Blindness and Contralateral Loss of Temporal Field

We have observed 2 patients who exhibited blindness in the homolateral eye and loss of the contralateral temporal field as the result of carotid obstruction. There was pronounced atrophy of the homolateral optic nerve and the contralateral nerve remained of normal color during a long period of observation.

Case 5. Progressive improvement in visual field of contralateral eye after thrombosis internal carotid artery.

T.T. (B.C.H. 47776 and 107802), a 60-year-old colored male, was admitted to Baltimore City Hospitals suffering from an acute left hemiplegia. He was said to have been completely blind in both eyes for a few days before admission. During that time the eyes were said to have deviated to the left.

There was elevation of blood pressure (160/120), an undetermined amount of

vision in the left eye, and a left hemiplegia more pronounced in the arm. Within a few days the blood pressure returned to normal limits.

At the time of first examination by one of us there was pronounced atrophy of the right optic nerve and the right eye was blind. The vessels were attenuated. The vision of the left eye was 20/20 and the fundus appeared normal. There was complete loss of temporal field of the left eye.

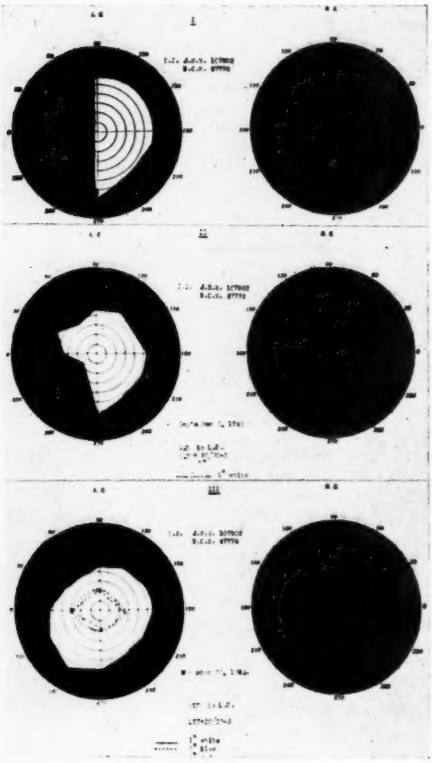


FIG. 5. *Case 5.* Visual fields. At onset the temporal defect in the left eye was complete. Then restoration of part of the upper field developed. Ultimately there was still further field improvement of the left eye.

Several months later the left arm remained spastic but the leg had regained normal function. There was a pronounced change in the visual fields (Fig. 5). After a further passage of several months there was even more recovery of the left visual field.

Several years after the patient was first seen death occurred and an autopsy was performed. An aneurysm involved the arch of the aorta and extended into the innominate artery; the aneurysm measured 11×8×7 cm. The common carotid artery on the right was completely thrombosed. [This case was reported by King and Langworthy[12] and by one of us (F.B.W.[22]) before autopsy had verified the diagnosis.]

Case 6. H.H. (520360), a 45-year-old man, in September 1947 noted occasional transient blindness of the right eye. Blood pressure was said to have been normal. Late in the same month he awakened one morning in a confused state and remained in bed for 10 days. He was told he had suffered a "stroke" affecting his left arm. On Nov. 1, 1947 he suddenly lost the upper half of his right visual field and weakness developed in the left arm. Gradually the weakness increased and affected the entire left side of the body. He enjoyed transient improvement and returned to work but 3 months later he had to cease work because of a return of the left-sided weakness. In May 1949 he had the first of three generalized convulsions beginning with twitching in the fingers of the left hand.

Examinations were made in November 1949. Visual acuity of the right eye was limited to counting fingers; the vision of the left eye was 20/15. The right optic disc was atrophic, the left was normal. A loss of the entire lower temporal field of

the left eye was found and was confirmed by one of us but unfortunately the field charts have been lost.

Percutaneous angiography was done on the right and only the external carotid vessels filled. Two days later a pneumoencephalogram showed a dilated right ventricle with an increased amount of air in the subarachnoid space. After a further week the right carotid artery was exposed and it was shown that the internal carotid artery was thrombosed. (This case was reported by Johnson and Walker.[10])

Homonymous Hemianopsia

It has been shown in Case 6 that a hemianopic field defect may change as time passes. Contralateral homonymous hemianopsia may appear and may remain only for a short time at the onset of the thrombosis (see Case 7).

Case 7. C.N. (534654), a 41-year-old white man, on March 9, 1950, complained of severe headache and inability to move his left arm and leg. The left side of the face was paralyzed. He remained conscious. The CSF contained blood. There was left homonymous hemianopsia. The headaches continued for several days and then improved and disappeared at the end of 2 weeks. The diagnosis on admission was subarachnoid hemorrhage probably resulting from rupture of an aneurysm.

Six weeks after the onset of his illness general examinations failed to reveal anything more than left hemiplegia. The CSF was normal. The vision was normal for both eyes and the visual fields were full. The fundi were normal save for low-grade retinal arteriosclerosis.

The right common carotid artery was exposed and the internal carotid was without pulsation and was seen to be thrombosed. Diodrast filled the external carotid system and $\frac{1}{2}$ cm. of the internal carotid artery. (This was reported by Johnson and Walker.[10])

Case 8. M.S. (B.C.H. 135638), a 43-year-old white female, 18 months before examinations were made, suddenly had a right hemiparesis, with mental confusion, motor aphasia and memory loss. For a week she suffered from minor convulsive episodes, each followed by inability to talk for an hour or more.

Examination showed the patient to be confused and with a marked memory defect. There was right-sided apraxia, tactile agnosia, nominal aphasia and alexia. The cranial nerves were normal save for right facial weakness of upper motor neuron type. The left pupil was larger than the right; both reacted to light. The paresis in the upper right extremity was more pronounced than in the lower. Deep tendon reflexes were increased on the right. Plantar responses were flexor. B.P. was 164/90. Serologic test for syphilis was negative. There was right homonymous hemianopsia.

A percutaneous injection of diodrast was made into the left common carotid artery. The external carotid system filled well and there was filling of $2\frac{1}{2}$ cm. of the internal carotid. Bilateral exposure of the common, external and internal carotid arteries was performed. There was fibrosis of the left internal carotid. A direct injection of diodrast was made into the right common carotid and there was adequate filling on that side and of the left anterior cerebral and the anterior communicating artery.

A recent examination showed pronounced general improvement. There was an

increase in the strength of the right side of the body. Memory was improved. The ataxia was improved and the alexia had in greatest part disappeared. The EEG showed improvement.

The right pupil was slightly larger than the left. Both reacted promptly to light. The ocular movements were of full range and there was no nystagmus. Vision was 20/30 and 20/40 in the right and left eye respectively. The optic fundi were normal. The visual fields (Fig. 6) contain a left homonymous defect which is incomplete above.

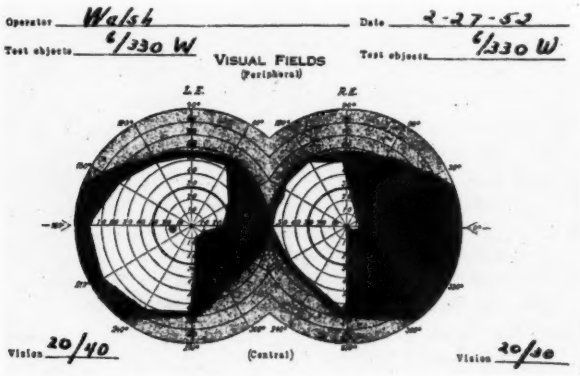


FIG. 6. *Case 8.* Visual fields.

Case 9. J.M. (U.H. 64354), a 54-year-old white man, was well until April 1950 when he suddenly became unable to speak. There was weakness of the right upper extremity with increased deep tendon reflexes on the right; also astereognosis and altered position sense. There was gradual improvement and the patient was able to go back to work. Quite suddenly in March 1951 there again developed pronounced weakness in the right upper extremity and he exhibited loss of memory. He was admitted on June 1, 1951.

There was pronounced weakness of the right upper and slight weakness of the right lower extremity. The right side of the face was paretic. There was subjective and objective hypesthesia over the right face and arm, and there was drooling from the right side of the mouth. Babinski and Hoffmann signs were present on the right. There was pronounced motor aphasia. Routine studies gave normal findings. B.P. was 160/90.

A left carotid arteriogram was made. It showed normal filling of the external carotid system and absence of filling of the internal carotid beyond 1 cm. distal to the bifurcation of the common carotid. A pneumoencephalogram showed atrophy of the cortex of the left hemisphere with compensatory left ventricular dilatation as has been observed in similar cases.

The patient was reexamined recently (Feb. 29, 1952). There was general improvement, but motor aphasia remained, also right spastic hemiparesis. The eyes appeared normal on external examination. The pupils were regular, equal and reacted sharply to light stimulation. The visual acuity was difficult to estimate but was quite good. The optic fundi appeared normal. The visual field contained a right homonymous defect, incomplete above (Fig. 7).

Case 10. J.B. (274786), a 58-year-old white male, was admitted to the Johns Hopkins Hospital after having had several convulsions. There was a long history of alcoholism and relatives stated he had been deteriorating mentally for several years.

Before admission he felt and acted normally but on admission he was drowsy. After a walk up a flight of stairs he looked blue, was tremulous and required assistance to reach a chair. He then fell backward to the floor and had a generalized convulsion with turning of the head to the right. After a few minutes he regained consciousness and was able to talk. Twenty minutes later he had another convulsion. A third convulsion developed as he reached the Accident Room.

On the following admission he became relatively clear mentally. Examination failed to reveal anything remarkable other than minimal signs of right hemiparesis.

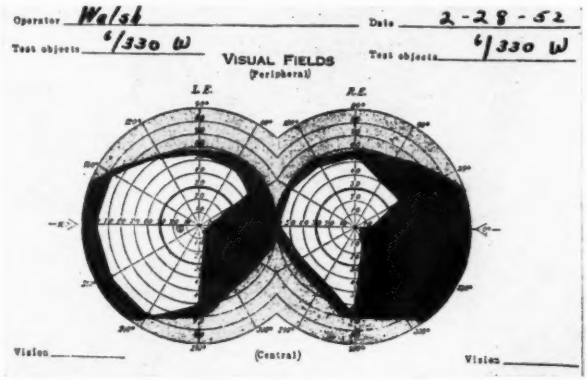


FIG. 7. *Case 9.* Visual fields.

The CSF was normal as regards pressure, protein and cell count. Blood serology for syphilis was negative. B.P. was normal. It was thought that alcoholism or intracranial tumor might be responsible for the convulsions. X-rays of the skull were read as normal. Examination of the eyes showed them to be normal externally. Visual acuity was 20/30 and 20/40-1 for the right and left eye respectively. The fundi appeared normal. There was a right homonymous hemianopsia with sparing of the upper quadrants (Fig. 8).

Left carotid arteriography was done by percutaneous puncture. The external carotid system filled but the internal carotid artery was not visualized. Further x-ray studies were undertaken. The right foramen lacerum seemed slightly larger than normal and no corresponding structure was visualized on the left. This suggested absence of the left internal carotid artery but several months later the artery was exposed and it was thrombosed. A right carotid arteriogram was made and in addition to normal filling on the right the left anterior and middle cerebral arteries were filled.

Comment. Homonymous field defects in these cases may be difficult to chart with exactitude. That homonymous hemianopsia may be transient is exemplified by Case 7. In Cases 5, 6, 8, 9, and 10 there is a striking similarity in the defective half-fields, namely a tendency to sparing of the upper quad-

rant. In Cases 5 and 6 there was optic atrophy homolateral to the thrombosis and normal optic discs in the contralateral eyes. In all cases of pure hemianopsia the discs were normal. In only 1 instance, Case 8, was there a possibility that pupillary size difference indicated tract involvement, but in this case curiously the pupillary size difference reversed itself. It would

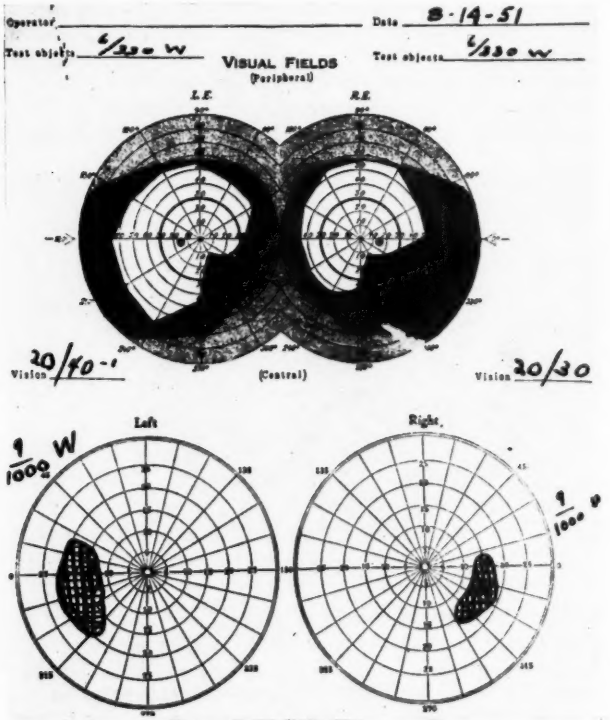


FIG. 8. *Case 10.* Visual fields.

seem that tract involvement is, at the most, incomplete in the cases here cited as exemplifying hemianopsia.

It has already been stated on the basis of arterial supply to the visual pathways that the evidence points to a preponderant involvement of the middle cerebral artery in these long-standing cases with hemianopsia. The reasons for this statement are as follows: (1) There would tend to be sparing of the lower homonymous half-fields if the arterial supply to the optic tract was interrupted (principally anterior choroidal also supplying the lateral aspect of the geniculate body, which receives fibers from the lower homonymous quadrants of the retina). (2) Involvement of the posterior choroidal artery would not be anticipated with thrombosis of the internal carotid ar-

tery other than when the posterior cerebral artery had its origin from the internal carotid artery. (3) If the anterior choroidal and posterior choroidal arteries are not affected then the middle cerebral, which supplies the radiation, remains as the probable site of obstruction. (4) In the instance of the posterior cerebral artery having an anomalous origin (which it seemingly has in possibly 25 per cent of cases [19,24]) the above deductions would not hold. (5) In any event the hemianopsia with sparing as shown in these cases probably represents arterial obstruction posterior to the tract.

Pupillary Abnormalities

Changes in the pupil have been described as associated with injection of contrast into the carotid artery. Similar but persistent pupillary changes are sometimes seen with thrombosis of the carotid artery. We have not seen either cases or records indicating pupillary changes associated with thrombosis of the external carotid artery. Johnson and Walker[10] found that in 107 cases of the type under consideration the homolateral pupil was fixed in 1, in 3 it was larger than in the opposite eye, and in 10 it was smaller than in the opposite eye.

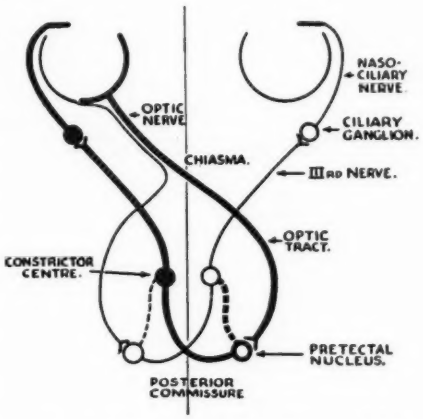


FIG. 9. Diagram from Duke-Elder explaining the wide pupil on the side of the hemianopsia in lesions of the tract. The fibers from the nasal retina which cross to the opposite tract are more numerous than are the temporal retinal fibers. Pupillomotor tone is accordingly less in the eye opposite the tract lesion. As a result the pupil on the side of the hemianopsia is larger.

An explanation for the small pupil is that there has been interruption to the sympathetic nerve either extra- or intracranially. Since the sympathetic fibers of the carotid plexus are available for involvement in all cases of thrombosis of the internal carotid artery it is not remarkable that narrowing of the pupils occurs rather often; it is remarkable that it occurs as infrequently as seems to be the case. What hemispheric involvement may have to do with narrowing of the pupil is not known. In a single instance (Case 11 summarized below) narrowing of the pupil associated with cranial nerve palsies served to provide accurate topical diagnosis.

When there is a wider pupil on the side contralateral to the thrombosis it is likely to be associated with a hemianopsia arising as a result of a tract involvement. In such an instance pallor of the discs would be anticipated but pallor certainly is not always present when the tract is the site of an extensive lesion (Fig. 9).

When the wide pupil is on the side of the thrombosis its wideness could

be explained as being caused by 3rd nerve palsy as is exemplified in our Case 12, in which thrombosis of the cavernous sinus provided for the palsy. Widening of the pupil may be explained on the basis of herniation of the cerebral hemisphere, as occurred in King's[11] case; in his patient infarction of the cerebral hemisphere produced swelling of the hemisphere with prolapse and pressure on the 3rd nerve. Finally it is possible that widening of the pupil might arise from stimulation of the sympathetic.

Case 11. Left-sided Horner's syndrome with involvement of 9th, 10th and 11th nerves and absence of long-tract signs suggested an extracranial lesion in region of carotid canal and jugular foramen. Left carotid arteriogram showed thrombosis of left internal carotid artery. This was later verified by surgical exposure. Thrombosis of left internal jugular vein.

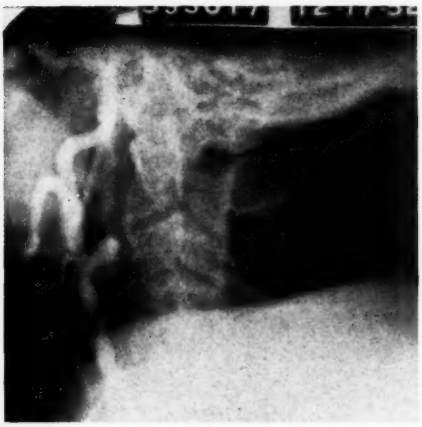


FIG. 10. *Case 11.* Left carotid arteriogram shows characteristic "nubbin" of internal carotid artery. This vessel often remains patent for approximately 1 cm.

J.W. (593017), a 51-year old Negro, complained of pain deep within the left ear. The pain spread to the region of the second upper molar tooth. The history as obtained from friends and relatives was not reliable.

In June 1951 the patient suffered a spell of unconsciousness and was admitted to a local hospital. Details regarding his stay there are not available. In August he had pain in the left ear. The pain was increased when he swallowed. Within a few days the pain radiated to the left upper jaw. He was then admitted to Johns Hopkins Hospital.

General physical examinations revealed nothing remarkable. Positive neurologic findings were: miosis on the left with low-grade ptosis; weakness of the left soft palate with reduced sensation in the left tonsillar region; absent gag reflex on the left; loss of sense of taste over the posterior third of the tongue; questionable loss of sensation over the left upper gum and swelling of the left parotid gland. Examination of the nasopharynx for tumor gave negative results. Roentgenograms of the skull seemed normal. The EEG low-voltage record exhibited a small amount of random slow activity.

A left carotid arteriogram was made (Fig. 10). The left internal carotid artery failed to fill but there was filling of the external carotid system. A pneumoencephalogram showed nothing remarkable. CSF and its pressure were normal. Compression of both jugular veins gave a prompt rise in CSF pressure but compression of the left vein did not alter the pressure.

Within a few days after the arteriography the patient seemed to improve and it was decided that verification of the thrombosis by surgical exposure was not justifiable. Two weeks after admission the patient was discharged. In a further 2 weeks he was reexamined. The pupils were of equal size but the left palpebral fissure remained very slightly narrower than the right. Several weeks later there was again

complaint of some pain in the region of the ear. Surgical exploration showed only internal carotid artery thrombosis and jugular vein thrombosis.

Ophthalmoplegia

Johnson and Walker[10] found mention of diplopia in a single case and ptosis in 6 cases among the 107 they included in their study. We have observed an interesting example of thrombosis of the carotid artery dependent upon cavernous sinus thrombosis and associated with ophthalmoplegia (Case 12).

It would seem reasonable that ophthalmoplegia associated with thrombosis of the internal carotid artery is usually caused by peripheral nerve involvement. Because of extensive hemispheric involvement in these cases conjugate palsies of supranuclear origin doubtless occur but we have not seen them. It is unlikely that nuclear palsies occur since the nuclei concerned with innervation of the ocular muscles receive their arterial blood from branches of the basilar and posterior cerebral arteries. This generalization regarding nuclear palsies would not hold good if the posterior cerebral artery was affected as a result of its having an anomalous origin from the internal carotid artery as shown in Fig. 2.

Case 12. A.B. (Mercy Hospital 109115), a 39-year-old Negro male, a known diabetic, was admitted to hospital in a disoriented state after having been found unconscious on the street.

The positive findings were: Pronounced proptosis of the left eye with edema of the lids; immobility of the eye and a semidilated and fixed pupil. Babinski's sign was present on the right. CSF pressure was 100 mm. water; the fluid contained 41 WBC, showed a 3+ Pandy reaction and contained 66 mg. per cent protein. X-rays revealed pansinusitis but clinical examinations failed to disclose an acute process.

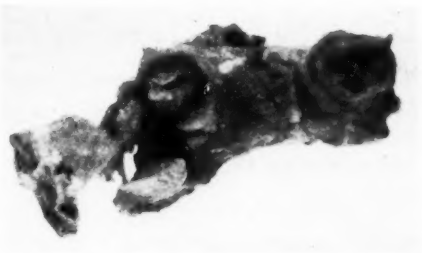


FIG. 11. *Case 12.* Autopsy specimen showing thrombosis of the cavernous sinus and thrombus plug in both ends of the carotid syphon. (Also see Figs. 3 and 4.)

Four days after admission a pronounced right hemiplegia developed with increased tendon reflexes on the right. Right-sided convulsions appeared. His state of consciousness, which had improved somewhat, became deteriorated. The optic fundi remained normal. The proptosis and immobility of the left eye remained unchanged but there was development of a 6th nerve paresis on the left. This indicated with more certainty a diagnosis of thrombosis of the cavernous sinus.

A left carotid arteriogram was made (Fig. 3). There was no filling of the internal carotid artery beyond the C2 level and the external carotid and its branches filled well. The right carotid was injected and there was filling of the homolateral external and internal carotid systems and good filling of the contralateral anterior and middle cerebrals (Fig. 4).

The patient ran a gradual downhill course and expired 2 weeks after admission to hospital.

Autopsy (Fig. 11) revealed thrombosis of the left cavernous sinus and thrombus filled the internal carotid artery within the sinus. The left anterior cerebral and middle cerebral arteries were patent.

Comment. This is an unusual case in which thrombosis of the carotid artery was dependent upon cavernous sinus thrombosis. It seems that such occurrences may be more frequent than we suspect when it is recalled that in some instances thrombosis of the carotid artery does not produce symptoms. With modern therapy the fully developed clinical picture of cavernous sinus thrombosis is rarely seen.

Papilledema

We have not seen papilledema in these cases. It seems probable that when papilledema occurs on the basis of increased intracranial pressure some factor other than thrombosis of the internal carotid artery is present. Possibly it is sometimes caused by an associated thrombosis of the dural venous sinuses. King[11] reported an interesting case of internal carotid artery thrombosis; lumbar puncture showed the spinal fluid pressure to be only 82 mm. fluid but 24 hours later there was greatly increased intraventricular pressure. Air injection revealed displacement of the ventricular system and a shift of the pineal as a result of swelling of cerebral tissue. Johnson and Walker[10] found mention of papilledema in only 2 of the 107 cases. Falls *et al.*[7] reported optic neuritis.

The Tonometric Syndrome

We do not have experience as regards the symptomatology described by Milletti.[15] He stated that pressure over the internal carotid artery contralateral to the thrombosis produces a reduction of the systolic retinal pressure of both eyes.

CONCLUSIONS

The ocular symptomatology associated with the injection of diodrast into the common carotid artery has been described. Seemingly the procedure holds an almost negligible threat as regards permanent loss of vision and transient loss of vision occurs rarely. Up to this time, so far as we are aware, no case of bilateral loss of vision has been seen as a result of angiography. Such a remarkable case of transient bilateral homonymous hemianopsia has been described.

Thrombosis of the internal carotid artery has been considered from the standpoint of its ocular symptoms and signs. Several cases have been included to exemplify these. What seems an observation of importance has been described in 5 cases of hemianopsia. In all there was a tendency toward sparing of the upper quadrant of the defective half-fields. From our studies of the arterial supply to the visual pathways it has seemed reasonable in

these cases to assume that the principal arterial obstruction occurred in the branch or branches from the middle cerebral artery to the optic radiation. Such a constant finding in the visual fields may have been merely chance but this possibility does seem unlikely.

Finally, this study indicates that further work regarding the vascular supply to the visual pathways should be worthwhile.

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OUR TRAINING PROGRAMS AND THE FUTURE OF NEUROLOGICAL SURGERY*

PAUL C. BUCY, M.D.†
Chicago, Illinois

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La vray science et le vray étude de l'homme, c'est l'homme.—Pierre Charron, 1601.

THE future of neurological surgery in North America lies in the hands of the members of this Society. This is neither a light nor a simple responsibility. The course of our specialty cannot, successfully, be allowed to find its own way. If the high level of clinical achievement, investigative progress and broad influence upon medicine generally, which our predecessors have set for us is to be maintained, it can be done only by constant effort directed by serious thought and consideration.

It is often difficult to recognize and assume responsibility that has been transmitted to us from older, revered hands. In neurological surgery we have been so very dependent upon the inspired leadership and able guidance of Harvey Cushing, Charles Elsberg, Charles Frazier, Walter Dandy, Max Peet and Alfred Adson, to name only those who are no longer with us. These men have very wisely directed the birth and development of neurological surgery and have maintained its intimate relationship to general surgery, anatomy, physiology and clinical neurology.

The responsibility to continue what they have begun is a complex one. There is no simple or single solution to the proper future development of this field, but the greatest single requirement is now and shall continue to be the providing of young men with stimulating leadership, attractive opportunities to work, to achieve and to grow, and ample time in which to do so.

Certainly the first demand upon us is that we provide competent men, adequately trained in clinical neurological surgery. That is not an easy task. It is not sufficient that we be content to teach young apprentices a trade. Ours is not a static field. No one of us can be satisfied with our present-day accomplishments. It is not enough that we teach only what we already know. We must prepare the future neurological surgeon to make new discoveries, to push neurological surgery to new frontiers. He must be prepared to appreciate and properly evaluate the discoveries and observations of others. He must be sufficiently conversant with the related fields of medicine and surgery that he can adapt and utilize the discoveries in other fields of clinical and basic sciences to his own work.

How can we best fit our residents to develop a better neurological surgery than we have today? We have already recognized that they have much to learn from the neighboring surgical fields, but what are we doing to insure

* Presidential address, meeting of the Harvey Cushing Society, Victoria, B.C., June 6, 1952.

† 25 East Washington Street, Chicago 2, Illinois.

that the greatest advantage is taken of the existing opportunities? Very little! We have recognized that these young men should be thoroughly grounded in the basic principles of surgery. But we have either felt that we ourselves are too deficient in our own knowledge of these principles or we have been too lazy to teach them. In any event we have insisted that the prospective resident come to us fully equipped in this regard by a year of training in general surgery. Surely it must be pike-staff plain that if these basic surgical principles are of importance to the practice of neurological surgery then any neurological surgeon worthy of conducting a residency should be thoroughly conversant with these principles and able to transmit them to his pupil. Obviously it would also be possible for the young man to learn these principles at the feet of a competent teacher of general surgery; but, what opportunity does he have to do so? Our present requirement of a year spent in general surgery is seldom a suitable way of attaining the desired end. It is often difficult for the prospective neurological surgeon to obtain the desired one-year residency in general surgery, and when he does obtain it, it is usually one of the poorer, less desirable residencies that he is awarded. It is perfectly natural that the best surgical residencies are not open to these candidates. The leaders in general surgery and the institutions with the best residency programs wish to concentrate their limited time and resources on men who will complete the full training program in general surgery and go on to leadership in that field. Men who spend only one year in a residency neither gain the most from the training nor contribute the most to the program. Thus the prospective neurological surgeon finds it necessary to accept one-year surgical residencies under men who are not particularly competent to teach and who are little interested in imparting surgical principles. These residencies are commonly in institutions prepared to offer a year of experience in the ordinary general surgical operations. Surely we are not interested in wasting a year of our prospective residents' valuable time in assisting at appendectomies, and cholecystectomies. Surely their time could be far better spent in learning basic surgical principles caring for neurosurgical patients and assisting at operations upon them. It seems most unfortunate that our present requirement fails to provide the training and experience that we all recognize as important while at the same time dissipating a year of the candidate's time to little advantage.

Demands made upon the neurosurgeon have created another problem. Neurological surgeons working in universities, large clinics and the bigger urban centers are able to call upon their neurological confreres for advice and assistance but as the younger men have gone into the smaller communities they have found not only that they have no neurological associates to call upon but that the local medical profession turn to them for assistance in the diagnosis and treatment of purely medical neurological disease. There are many obvious reasons, which we shall not discuss, why a neurological training is of importance to a neurological surgeon, but the simple practical points that have been mentioned here are of themselves sufficient reasons

why we should insure that the prospective neurosurgeon have an adequate neurological background.

Most of us recognize that one of the most valuable parts of the training program of any resident lies in his contact with others training in his own and related fields. The resident in neurological surgery can learn and benefit much from his contacts and discussions with residents in general surgery, as well as the other fields of medicine and surgery. All too frequently, however, our training programs are established in isolated institutes devoted exclusively to neurological surgery, where the residents have little or no opportunity to attend the staff meetings in other fields, the general clinico-pathological conferences or the meetings at which research in the basic sciences is presented. This isolation of the student is certainly most undesirable from the standpoint of creating in him a broad viewpoint and knowledge.

I mentioned a moment ago the serious matter of wasting the time of young men in training in neurological surgery. This is probably the most serious matter confronting us. Time and youth are the two things that they can so easily lose but can never regain. The one thing above all others that is essential to the advancement of this or any other field is ideas. And the time when ideas appear most prolifically is when men are young. It is young men with active inquiring minds, unhampered by tradition or the "knowledge" that "it can't be done," who are most likely to bring a fresh, vigorous, worthwhile viewpoint to a troublesome problem. This was again brought forcefully to my attention as I stood last Autumn in the old anatomical amphitheater of Olof Rudbeck at the University of Upsala in Sweden. Rudbeck was one of the many men who have made important contributions to human knowledge early in life. At 18 years of age he enrolled in the University, and almost immediately began his biological investigations which led to the discovery of the lymphatic system and disproved the previously held opinion that the blood is formed in the liver. In April 1652, at the age of 22, Rudbeck demonstrated the lymphatic system which he had recently discovered to Queen Christina in the anatomical amphitheater and in the following month defended his thesis on "The Circulation of the Blood" (*De circulatione sanguinis*) before the faculty. Although the achievements of Rudbeck are among the outstanding examples of the scientific accomplishments of young men, it is not to be assumed that significant accomplishments are possible only to young men of years gone by. They are still possible if we but give young men the opportunity. However, we can not expect them to make real contributions to our knowledge if we persist in encasing them in educational straight-jackets, demanding that all of their time be spent in primary, collegiate and medical school education until they are 25 or 26 years of age and that they then spend the next five to seven years in a rigidly controlled residency program.

It is, of course, obvious that not all men who are interested in neurological surgery and capable of becoming able surgeons in that field are interested in or will benefit by training and experience in basic research. Such

men should not have research experience thrust upon them. On the other hand, we must not make our requirements so rigid that those who are capable and are interested will be denied the opportunity of such training in investigation. We must never forget that training in research has a two-fold advantage. There are a few men who will make important discoveries and will go on to become leaders in the field of neurological investigation. Unfortunately the number of such men is not great. However, training in basic research is of value not only to these select few. It can be of the greatest value to those who will carry on clinical research and clinical observation. All too many of those who publish on clinical subjects have little appreciation of the scientific method, or its inherent importance in the evaluation of clinical observations. They fail to appreciate the importance of adequate controls, and of multiple observations. They often do not recognize the difference between those statistical variations that are insignificant and those that are valid. The most profitable way in which to correct these deficiencies and to improve the level of clinical research in the field of neurological surgery is to extend the opportunity for basic research under leaders with a thorough understanding of scientific principles. Furthermore, it is of importance to the advancement of neurological surgery that its devotees be thoroughly conversant with developments in the basic neurological sciences and be sufficiently well trained in scientific methods to evaluate and understand the works of others in these fields.

It is also of importance that interest in research into the structure and function of the nervous system be kept alive among neurological surgeons. Only in that way will our specialty remain alive as a vital growing field of medicine. Furthermore, there are many problems in the field of fundamental neurology that can be investigated only by or through the active cooperation of a neurological surgeon. There is no part of the body that varies so widely from that of the laboratory animal as does the human brain. Although studies of the structure and function of the animal brain are of great importance they can only point the way to conclusive human research. No fact found to be true for the central nervous system of lower animals can be finally accepted as true of the human brain and spinal cord until it has been proved true for man. Many parts of the human brain are not duplicated in the brains of dogs, cats and monkeys; many human diseases find no counterpart in lower animals. If these are to be understood it will be only through the study of man himself.

As neurosurgeons we have a heritage from the past and an obligation to the future which we must never permit ourselves to forget. Among our obligations is that of advancing the science of our own particular field. Like those who devote their lives to basic science or to "pure" science we must never permit this obligation to become confused with the question of the practical value of our observations. Truly scientific observations must be pursued for themselves alone.

Recently I have been impressed with the significance of this as I read

the beautiful and detailed clinical and postmortem studies and correlations of Abercrombie in "Diseases of the Spinal Marrow" which was published in 1818, of Andral in his classical description of two cases of subdural hematoma which he observed in 1822, and of William Gull in his extensive studies of the causes of paraplegia which were reported in Guy's Hospital Reports for 1858. These men had no thought of the practicality of these observations. Within the confines of their vision these were incurable conditions and there was no reason for them to hope that they would ever be otherwise. It was not until many years later in 1884 that the first tumor of the brain was localized by purely neurological means and operated upon, and two years later in 1886 that Horsley, much against the advice of many of the leading surgeons of England, first operated upon a tumor of the spinal cord. Yet it would have been impossible to have carried out these operations without these and other earlier studies.

I would be grossly misunderstood if it were thought that I were pleading here for extensive research experience and training in the basic neurological sciences and clinical neurology for all prospective neurological surgeons. That is not the case. My plea is that our requirements be kept flexible so that each candidate may vary his training program to include such of these fields of related activity as he finds interesting and profitable. We will have candidates come to us with a broad training in general surgery, far beyond that which is now required as a minimum. The value of that background should be recognized and such candidates should not be expected to present as full a program of training in other fields as is expected of others. The excellence of such a training program is adequately demonstrated by the outstanding neurological surgeons who received their training as part of the residency in general surgery at the Johns Hopkins Hospital with their neurosurgical training under the guidance of the late Walter Dandy. Likewise, men who have spent their early years in the laboratories of neuro-anatomy and neurophysiology and the clinics of diagnostic neurology should receive credit for that training, provided their neurosurgical training has been at the hands of a competent surgeon. An outstanding example of the value of such a background is the late Clovis Vincent, who was responsible for much of the modern resurgence of neurological surgery in France.

It is no accident that neurological surgery has had leaders of exceptional ability. Men who have been called upon and given distinguished service in fields beyond the confines of our specialty; heads of departments of surgery and neurology, directors of institutes, leadership in our national societies in general medicine and surgery. This is a tribute to their inherent abilities and their broad training and outlook. We have been fortunate in that the men who have constituted our specialty board have wisely recognized the importance of keeping the requirements for certification at a minimal level and very flexible. We must see that they remain so. There are constant pressures upon the board to make their requirements more exact, to introduce didactic courses which the prospective candidate must follow, to define the number

of hours that must be spent in each field. It is not always easy to resist these pressures but it is of the greatest importance that we do so. We must never permit any agency to cast the training of our young men in rigid molds. The future of neurology and neurological surgery lies in these young men, in their activities during their early years and in their training. Their opportunities, their energies and enthusiasms and their years must never be wasted.

CASE REPORTS AND TECHNICAL NOTES

ANEURYSM OF ANOMALOUS OPHTHALMIC ARTERY

PRESENTING IN THE SPHENOID SINUS AND SIMULATING AN ANEURYSM OF THE INTERNAL CAROTID ARTERY ON ROUTINE ARTERIOGRAPHY

GORDON J. KINLEY, M.D., AND DAVID S. LEIGHNINGER, M.D.

Department of Surgery, Western Reserve University School of Medicine and University Hospitals of Cleveland, Cleveland, Ohio

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Epistaxis as the presenting symptom of aneurysms or arteriovenous fistulae in the region of the sphenoid sinus has been mentioned in at least 3 other cases.[1,2,3] The diagnosis was based upon the occurrence of arterial epistaxes and an associated bruit, or adjacent cranial nerve palsies. In none was the aneurysm demonstrated by contrast radiography. Two of these patients were cured by carotid ligation [2,3] but the third died of the epistaxis.[1]

CASE SUMMARY

Case #288-991. A 42-year-old colored female was admitted to the emergency ward on Oct. 13, 1949 within 1 hour following an automobile accident in which her head struck the dashboard.

She had sustained multiple lacerations of the face, bilateral fractures of the mandible and a compound comminuted depressed fracture of the right frontal bone involving the entire supraorbital ridge, right frontal sinus and roof of the orbit.

Examination. There was complete anesthesia of the right forehead and cheek. The right eye was completely blind, deviated upward and outward, and the pupil was ovoid and fixed. Funduscopic examination revealed venous engorgement but no hemorrhages in the right retina. The left eye was normal. Cerebrospinal rhinorrhea was not evident.

Motor power and coordination of all extremities were good. The deep tendon reflexes were generally hypoactive and there was a left positive Babinski. There was no evidence of intrathoracic or abdominal injury.

1st Operation. Following preparation with blood transfusion, penicillin, tetanus antitoxin and atropine the patient was taken to surgery. The wounds were debrided, grossly contaminated bone fragments were removed, lacerations of the dura were repaired, and the right frontal sinus was curetted and packed with gelfoam and gauze. The incisions were closed primarily and the gauze pack was brought out through the lateral end of the supraorbital incision. The head dressing was adapted to also immobilize the jaw fractures.

Course. Postoperatively she was placed on chemotherapy and tube feedings. The packing was removed on the 6th and the sutures on the 8th day. More nearly accurate reduction of the mandibular fractures was secured by means of Jelenko splints. When discharged on her 23rd postoperative day there were anesthesia and a soft depression of the right forehead, blindness of the right eye and weakness of the right 3rd nerve.

She was followed in the out-patient department where the Jelenko splints were removed, and the 3rd nerve weakness recovered completely. During this time she also had been treated in the emergency ward for 3 episodes of epistaxis.

The otolaryngological service readmitted her to the hospital on Dec. 3, 1949 for investigation of these epistaxes. Nasopharyngoscopy revealed the source of the bleeding to be the sphenoid sinus. In an attempt at lipiodol instillation, cannulation of the sphenoid ostium resulted in brisk arterial bleeding through the cannula.

Right percutaneous carotid arteriography on Dec. 15, 1949 revealed an ovoid midline

opacity below and anterior to the sella turcica which apparently arose from the right internal carotid artery (Figs. 1 and 2). An oblique view, however, showed this opacity to have an elongated stalk connecting it with the internal carotid artery close to the posterior genu (Fig. 3).

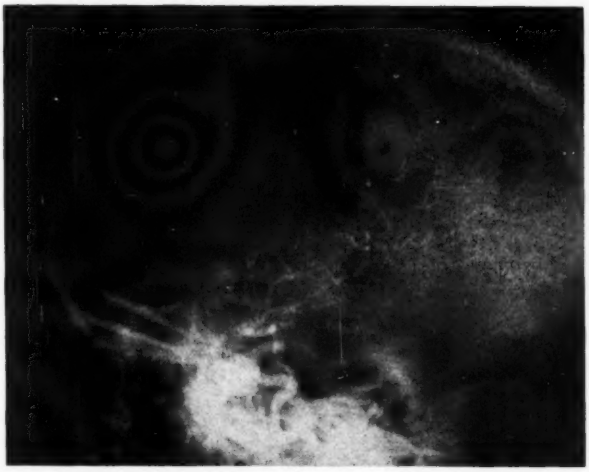


FIG. 1. Carotid arteriogram. Right lateral view. Arterial phase showing the globoid well defined collection of dye anterior to the sella turcica, apparently continuous with the internal carotid artery.

FIG. 2. Right lateral view. Venous phase showing the persistence of dye in the aneurysmal sac beyond the arterial phase.

2nd Operation. On Dec. 19, 1949, following a 15-minute trial occlusion of the right internal carotid artery under local anesthesia, it was permanently ligated 2 cm. distal to the carotid bifurcation in the neck.

3rd Operation. Two weeks later a right frontal osteoplastic flap was reflected and two silver

clips were placed across the internal carotid artery where it emerged from the cavernous sinu (Figs. 4 and 5). The ophthalmic artery was not visualized; however, pulsations present in th internal carotid artery ceased proximal to the clips.

Course. The patient made an uneventful recovery and subsequently returned for a tanta-

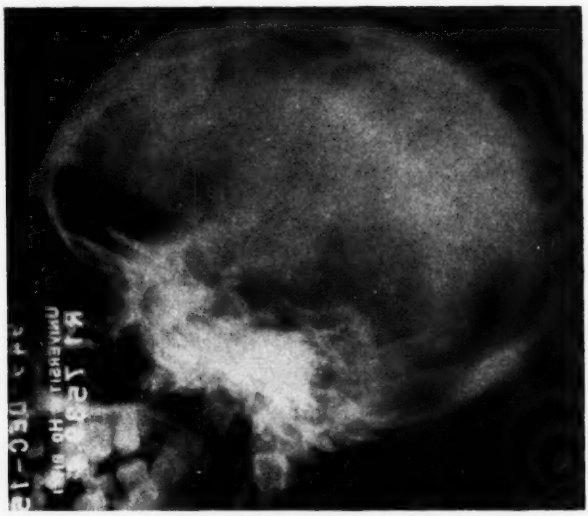
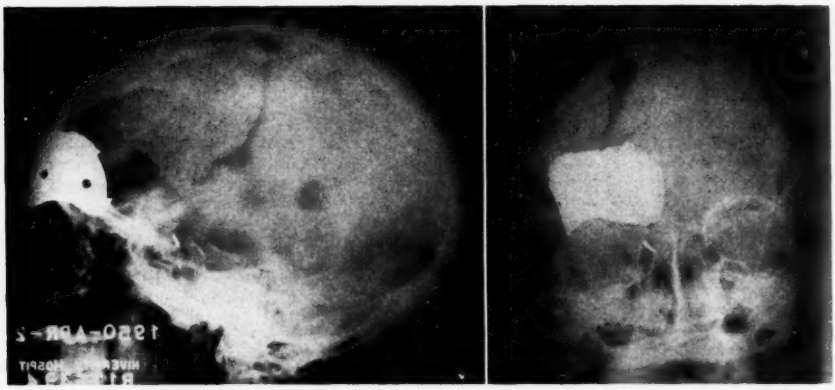


FIG. 3. Left anterior oblique view. Arterial phase showing the continuity of the aneurysm and what is taken to be an anomalous ophthalmic branch of the internal carotid artery.



FIGS. 4 and 5. Lateral and anteroposterior views showing tantalum cranioplasty and the clips on the intra-cranial portion of the internal carotid artery where it emerges from the cavernous sinus.

lum cranioplasty (Figs. 4 and 5) to correct the defect of the supraorbital ridge and forehead. The blindness of the right eye persists and primary optic atrophy is now evident. There ha- been no recurrence of the epistaxis and she has made an excellent adjustment to her duties a- a housewife 2 years postoperatively.

COMMENT

Epistaxis complicating a severe head injury is not unusual but when it occurs weeks later its direct relation to the injury is not so apparent.

The differential diagnosis of a neoplasm, arteriovenous fistula or aneurysm was greatly simplified by the right carotid arteriogram which showed a saccular midline aneurysm located anteroinferior to the sella.

The term aneurysm is used because of the density of its contained dye, globoid outline, sharply defined margins, the lack of a venous exit, and its continuity with the internal carotid artery.

The routine lateral and anteroposterior arteriogram views at first suggested an origin from the right internal carotid artery. In an attempt to better define the neck of the aneurysm a left anterior oblique view was made; this revealed an unusually long narrow stalk which was taken to be the ophthalmic branch (Fig. 3).

The ophthalmic artery in this instance arose quite far posteriorly in the cavernous sinus rather than at its usual site of origin at the anterior genu of the internal carotid.

Revascularization of this "trapped" aneurysm via the ophthalmic artery was felt to be unlikely in view of the cessation of pulsation in the isolated segment of the internal carotid artery.

In this particular case the coincidence of the blindness, optic atrophy and aneurysm of the ophthalmic artery following the accident suggests the possibility of an unrecognized fracture involving the lesser wing of the right sphenoid, optic foramen and adjacent sphenoid sinus.

SUMMARY

1. A case of traumatic aneurysm of the ophthalmic artery is summarized.

2. The use of an oblique view in angiography to accurately identify the origin of this aneurysm is illustrated.

3. Indirect control of the aneurysm is outlined.

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TRANSIENT LOSS OF VISION FOLLOWING CEREBRAL ARTERIOGRAPHY

Frank J. Otenasek, M.D., and James Markham, M.D.
Division of Neurological Surgery, Johns Hopkins Medical School and Hospital, Baltimore, Maryland

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Not a few descriptions of the various complications of cerebral arteriography may be found in the literature, but those related to disturbance of vision have been rare. The authors deem it worth while to record a case in which there was marked reduc-

tion in vision on the injected side within 2 hours of arteriography and complete recovery within 48 hours. The development and course of this phenomenon appeared to be directly related to the arteriographic procedure.

CASE REPORT

J. H. H. No. 591170. A 51-year-old white male from Texas was admitted on the service of Dr. Benjamin M. Baker with hemiparesis of 2 years' duration. The family history was not remarkable except that the patient's mother had been diabetic, although the cause of her death was unknown. The past history was not contributory.

At the age of 40 years, or 11 years before admission, the patient had an episode of left facial palsy, weakness of the left arm, and pain in the left side of the neck. These symptoms lasted only half a day, then disappeared completely; but following that episode he had noted loss of temperature appreciation on the left side of his body.

In May 1949, or 9 years later, he had weakness of the 4th and 5th fingers of his left hand lasting for 2 or 3 days. In June 1949, he awoke one morning and found his left arm paralyzed. Within the next 3 days a flaccid hemiplegia developed, without involvement of the face and with no headaches or loss of consciousness. During the following 6 months strength returned gradually, walking was resumed, and it became possible for him to use the arm and hand to a surprising extent.

In October 1951, 1 month prior to admission, he began to stagger one day and his tongue became awkward but within 12 hours these symptoms disappeared.

Examination. On admission, temperature, pulse, and respiration were normal. Blood pressure was 136/82. He appeared quite healthy but slightly overweight. The eyes, ears, nose, and throat were normal. The thyroid was not felt and there was no lymphadenopathy. Lungs were clear to percussion and auscultation. The heart was normal in size and the rhythm was good. No murmurs or irregularities were noted. The abdomen was soft, somewhat protuberant, and the liver, kidneys and spleen were not palpable. The prostate was normal in size and consistency. Peripheral blood vessels did not seem sclerotic.

Neurologic examination revealed that the pupils were equal, round, and reacted well to light, accommodation and consensual stimulation. There was a full range of ocular motility and nystagmus was not observed. The optic discs were flat, with sharp neuroretinal margins and distinct laminae cribrosae. Retinal vessels were not noticeably narrowed. Facial movements were symmetrical and facial sensation was normal to testing. He walked with some difficulty, dragging the left leg slightly, while associated coordinated movements in the left arm were lacking. Muscular tone seemed equal on both sides but strength was moderately decreased on the left. Tendon reflexes were exaggerated on the same side, and the plantar response was extensor on the left. Abdominal reflexes were present and equal. Clonus was not elicited, nor was the Hoffmann sign. Finger-nose and heel-knee tests were poorly executed on the left, while fine movements were not possible with the left hand. Sensory examination revealed hypesthesia and hypalgesia with impaired temperature appreciation over the left side of the body below the clavicle. Vibratory and position sense, however, were unaffected, and the Romberg sign was negative.

Laboratory Data. Hb. 16.0 gm. WBC 6100 with normal differential. Erythrocytes and platelets normal on smear. Sedimentation rate 18 mm. (corrected). Icterus index 3.0. NPN 30.0. Blood cholesterol 306. Urinalysis revealed a trace of albumin. X-rays of the skull were normal.

Arteriography. On Nov. 26, 1951, percutaneous carotid arteriography was performed on the right side under local anesthesia. One hour previously, he had been given phenobarbital (96 mg.) and demerol (150 mg.) subcutaneously. The preliminary conjunctival sensitivity test using 2 drops of diodrast (35 per cent) was negative. Stellate ganglion block with 1 per cent procaine was carried out prior to dye injection and a good Horner's syndrome developed. Carotid puncture was done two fingers above the clavicle and performed without difficulty. A good exchange was obtained. Four injections of 15 cc. each (total 60 cc.) of 35 per cent d[iodrast]

drast were made for stereoscopic AP and lateral views. The lateral films showed the external carotid system was well filled but no dye appeared in the internal carotid intracranially or in the neck. In the A-P views, at the level where the internal carotid arises in most cases, there is a bare suggestion of an occluded internal carotid but the course of the dye was smooth and unbroken in the external.

Course. Immediately after the last injection the patient complained of slight burning of the right side of his face and slight supraorbital aching. He was returned to his room on a stretcher and fell asleep. Upon awakening 2 hours later he discovered the vision in his right eye was greatly impaired and he could distinguish only large objects. He also noted aching of the right globe and in the right supraorbital region.

Examination made 4 hours after the injection showed the Horner's syndrome had disappeared. There was a large central scotoma of the right eye which was absolute for a 5 mm. white object at 1 foot and incorporating the blind spot. Peripheral fields were constricted but the nasal loss was greater. Visual acuity was limited to counting fingers at 1 foot. On funduscopic examination, the right disc was of normal color. The neuroretinal margins were slightly blurred nasally and superiorly. Arterioles were smooth and of normal caliber, while the veins were not overfilled. The macular area appeared rather unusually reddened and indistinct but no hemorrhages, exudates, or sludging were noted. The appearance of the left fundus was similar except there were no corresponding alterations in the macular area.

Four hours later, or 6 hours after the arteriography, vision was unimproved. A stellate ganglion block was done at this time with 1 per cent procaine. Thirty minutes later the patient volunteered the information that his vision was improving. When seen again 16 hours after the onset of visual loss he stated vision had continued to improve and examination revealed he could read large letters and the scotoma was much reduced in size. Another stellate block was done at this time. Twenty-one hours after the onset of visual symptoms, the scotoma was not elicited and peripheral fields were but slightly constricted. The right fundus showed marked decrease in the swelling of the macular area. Visual acuity at this time was equivalent to 20/40 on the right. A third (and last) stellate block was then done.

An ophthalmological examination by Dr. Frank Walsh at the end of 48 hours after the onset of visual symptoms revealed the fundi to be normal in appearance. Central and peripheral fields were quite full and no scotomata could be demonstrated with 3/1000 white, red and blue objects.

Further diagnostic procedures were foregone and a repeat arteriogram was considered inadvisable at this time. A letter has been received from the patient, dated Feb. 23, 1952, in which he states his vision is perfectly normal.

DISCUSSION

Clinically, the case just described could be regarded as one of recurring cerebral vascular occlusions. On the basis of the arteriogram alone, thrombosis of the internal carotid artery could not be established with absolute confidence. The lack of filling of this vessel could have been due to congenital absence of the internal carotid, a condition which Dandy[3] had observed, or to spasm or thrombotic occlusion immediately above the bifurcation of the common carotid.

At least the transient visual failure must be considered a complication of the arteriographic procedure, occurring as it did within 2 hours afterward. What mechanism was responsible for this unusual reaction is not entirely clear. Embolism or thrombosis of the central retinal artery or vein or of a retinal vessel can be excluded on the basis of the funduscopic examinations and such complete recovery.

That spasm may have contributed cannot be excluded. Ecker and Riemenschneider[7] have presented clinical evidence of such a phenomenon related to cerebral arteriography. An anomalous origin of collateral supply of the ophthalmic circulation from the external carotid or the middle meningeal, as mentioned by Walsh,[13]

with spasm of the supplying vessel could have resulted in such a phenomenon.

Transient spasm of the ophthalmic or its derivative would result in temporary anoxia of the retina. Noell and Chinn[11] have shown experimentally in electroretinographic studies on rabbits that transient anoxia produces significant changes in the optic tract potentials.

That sensitivity to diodrast could be a factor was apparently excluded by the negative conjunctival test. In any case it seems extremely unlikely that such a discrete, unilateral alteration of vision could be explained on an allergic basis alone.

The complications of cerebral arteriography reported in the literature are numerous and include urticaria,[12,15] fever,[12] local reactions in the neck,[6,15] cervical sympathetic palsy,[5,15] recurrent laryngeal nerve paralysis,[6] vomiting,[6,15] hemiplegia (total or partial, permanent or transitory)[1,4,5,6,8] convulsions,[5,6,8,9] aphasia,[6,9] air embolism,[10] thrombosis of the internal carotid artery[8,12] and rarely, fatal outcomes.[5,8,9]

Weekers[14] reported a case of occlusion of a retinal artery following cerebral arteriography. In his case there was a convulsive seizure immediately afterward, followed by hemiplegia which abated. The next day the patient noted a superior field defect in his right eye. Visual fields showed a superior nasal quadrant defect and a large zone of white edema in the submacular region of the right eye. There was permanent loss of vision in the affected quadrant. Weekers considered that embolism was most likely responsible and due to a floating blood clot, fragment of tissue, or dislodged atheromatous plaque.

Curtis[2] described a case of focal seizure on the contralateral side following arteriography and brief loss of consciousness. Later in the same day, the patient noted some impairment of vision. Ophthalmologic examination 2 days after the injection revealed spasm of the retinal arterioles and a central scotoma which did not resolve.

Falls, Bassett and Lamberts[8] mentioned 2 cases of visual loss following arteriography. In 1 case this lasted but 10 minutes and in the other for 30. Neither case was studied during the period of visual loss however and ophthalmologic examinations were negative.

In a series of more than 700 cerebral arteriographies which have been conducted at this hospital since 1948 no similar complication has occurred.

SUMMARY

A case of transient visual failure following cerebral arteriography is described. This was characterized by unilateral central scotoma on the injected side with constriction of peripheral fields occurring within 2 hours after injection of 35 per cent diodrast and with complete recovery within 48 hours. The possible mechanisms responsible for this reaction are discussed. Therapeutic stellate ganglion block with 1 per cent procaine may have been beneficial. When impairment of vision occurs following cerebral arteriography and there is no ophthalmologic evidence of vascular alteration the prognosis for restoration of vision is probably favorable.

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DOUBLE-JOINTED TANTALUM-CLIP-APPLYING FORCEPS

Albert S. Crawford, M.D.*
Neurosurgical Division, Henry Ford Hospital, Detroit, Michigan

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It seemed to us some years ago that there was need for an instrument to apply silver or tantalum clips at various angles with a longer handle than the Cushing and McKenzie models and increasing the power by making it double-jointed. The in-

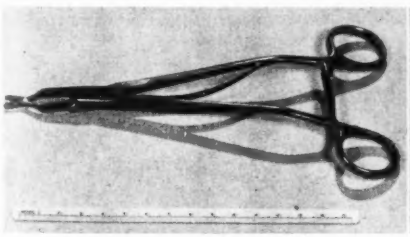

Fig. 1.

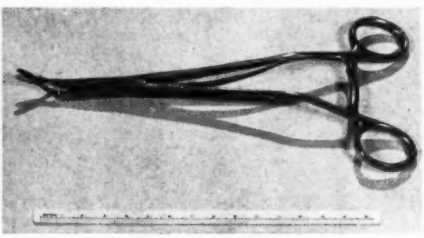

Fig. 2.

strument herein described not only met the above requirements, but, in addition, supplied a more secure grip upon the clip. It has been used by us and has proven its usefulness for a number of years. The three models commonly used are shown here. The first (Fig. 1) has a straight tip; the second (Fig. 2) has an offset tip and the

* 173 Main Street, Waterville, Maine.

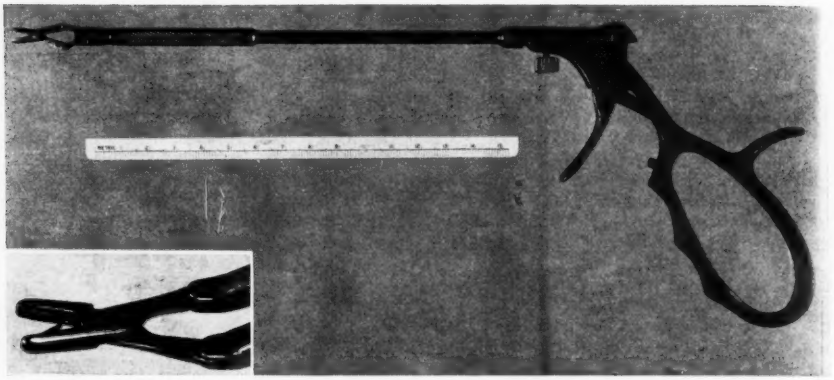

FIG. 3.

third (Fig. 3) is a longer forceps with a pistol grip. The first two are $7\frac{1}{4}$ inches long and the third is $11\frac{1}{2}$ inches long. The inset in Fig. 3 shows the clip and its retaining features in better detail.

The forceps are made of stainless steel.*

* The instruments are manufactured by Alfred H. Schmitt, 38105 Woodcrest Drive, R.R. #5, Mt. Clemens, Michigan.

NOTICES

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

The annual meeting of the Association for Research in Nervous and Mental Disease will be held on December 12 and 13, 1952 at the Hotel Roosevelt, New York City. The subject of the meeting will be "Metabolic and Toxic Diseases of the Nervous System."

CHARLES A. ELSBERG LECTURE

Dr. Herbert Olivecrona, Professor of Neurosurgery, Stockholm, Sweden, will deliver the Annual Charles A. Elsberg Lecture, established by the New York Society of Neurosurgery, on December 1, 1952 at the New York Academy of Medicine, 2 East 103rd Street, New York City, at 8:30 P.M. Dr. Olivecrona has chosen for his subject, "Hypophysectomy in Man."

CONGRESS OF NEUROLOGICAL SURGEONS

The second annual convention of the Congress of Neurological Surgeons will be held at the Palmer House, Chicago, Ill., November 6–7, 1952. A symposium on Peripheral Vascular Diseases will be presented by Drs. Albert Kuntz, St. Louis, E. A. Hines, Jr., Rochester, Minn., and Bronson Ray, New York. A symposium on Headaches will be presented by Drs. Albert Kuntz, F. L. McNaughton, Montreal, Harold G. Wolff, New York and Bronson Ray.

Professor Herbert Olivecrona of Stockholm, Sweden, will present three addresses: "The Treatment of Arteriovenous Aneurysms of the Brain," "The Treatment of Aneurysms of the Circle of Willis," and "Hypophysectomy in Man."

A round-table discussion of "Pseudo-tumor Cerebri and Treatment of Gliomas" will also be presented. The panel for this discussion includes Drs. Percival Bailey, Loyal Davis and Eric Oldberg, all of Chicago, Dr. Ray and Prof. Olivecrona.

Anyone interested in attending this convention can make arrangements with the Secretary, Dr. Bland W. Cannon, 1092 Madison Avenue, Memphis, Tennessee.

INTRACRANIAL TUBERCULOMAS

EXPERIENCE WITH TEN CONSECUTIVE CASES

ANTONIO GONZÁLEZ-REVILLA, M.D.

Instituto de Neurocirugía Walter E. Dandy, Hospital Santo Tomas, Panama, R. of P.

(Received for publication May 16, 1952)

TUBERCULOMAS are among the common expanding intracranial lesions. Their incidence varies according to their geographical distribution. Thus in a series reported from the United States[14] tuberculomas represented 1.4 per cent of all verified intracranial tumors, and in a report from Chile[1] the incidence was 15.9 per cent. It is said that the incidence is higher in children than in adults[1,5,8] and higher in males than females.[3,8]

The symptoms and signs of this type of lesion do not differ from those caused by other kinds of intracranial tumors. Asenjo *et al.*[1] have called attention to the high incidence of intracranial hypertension in their series of cases, but they do not state the criteria used for increased intracranial pressure and their graphs are hard to interpret. Even in the presence of extracranial tuberculous lesions it is quite difficult to make a preoperative diagnosis of tuberculoma; hence it is unwise to treat these patients by decompressive measures alone without knowing beforehand the pathological nature of the lesion.

Before the advent of streptomycin, the surgical treatment of cerebral tuberculomas was discouraging because of the common occurrence of postoperative tuberculous meningitis. The poor results from this dreaded complication led Cushing[5] to recommend decompression followed by general medical care as the therapeutic method of choice, although he warned against the danger of overlooking nontuberculous lesions by this procedure. On the other hand, Dandy,[6] Dott,[7] and Smith and Daniel[13] advocated total removal of the lesion whenever its anatomical location made it feasible. Dandy advised the same surgical extirpation *en bloc* as used in the treatment of a glioma with a margin of healthy cerebral tissue around it. Scattered reports have appeared in the literature on the results of surgical extirpation combined with streptomycin administration in the past 3 years.[1–4,9–12,15] Sufficient follow-up observation was found only in the cases reported by Obrador and Urquiza[10] who emphasized that 1 out of 4 patients with cerebral tuberculomas survived the surgical extirpation alone, while in a series of 6 patients treated surgically and with streptomycin, 1 died postoperatively and 5 were well from 12 to 18 months after operation.

The purpose of the present communication is to discuss our personal experience in 10 consecutive cases of intracranial tuberculomas verified at operation or autopsy in our Department of Neurological Surgery. Emphasis will be placed on incidence, symptomatology, operative findings, treatment and end results.

INCIDENCE AND DURATION OF SYMPTOMS

In our series tuberculomas constitute 8 per cent of all intracranial tumors verified at operation or autopsy. From 1948 to 1951 there were 10 such cases. Females were affected more frequently than males in the proportion of 3:2. The average age at onset of symptoms was 21.5 years; the youngest patient was 3 years old, and the oldest 54. Fifty per cent of the tuberculomas occurred in children under 14 and the other 50 per cent in adults over 20. The duration of symptoms in 7 cases fluctuated between 2 and 3 months, while in the rest it was 7, 24 and 36 months respectively. There was no significant predilection for racial groups; 4 occurred in Indians and 3 each in white and colored individuals.

TABLE 1

Incidence and duration of symptoms

Case No.	Hosp. No.	Age (years)	Race	Sex	Duration of Symptoms (months)
1	414.527	7	Colored	M	7.0
2	419.660	28	Indian	F	36.0
3	420.560	10	White	F	2.5
4	453.900	14	White	F	2.0
5	454.259	51	Colored	F	3.0
6	454.632	3	Colored	M	2.0
7	457.977	20	Indian	F	24.0
8	460.152	54	White	M	2.0
9	472.727	3	Indian	M	2.0
10	481.795	24	Indian	F	2.0

SYMPTOMS AND SIGNS

Of the 10 tuberculomas, 9 were intracerebral and 1 was epidural. Because of some difference in their symptomatology they will be discussed under separate headings.

(a) *Intracerebral.* Among the 9 cases in this group there was history of fever as the initial symptom in 3, the temperature fluctuating between 101° and 103° and lasting for 8 days. No symptoms or signs of meningitis could be obtained from their histories.

Headache was a prominent and constant symptom in every case. It was described as severe, intermittent and generalized, irrespective of the location of the lesion, and was associated with vomiting in 5 cases.

Convulsive seizures were present in 4 patients in whom the tuberculomas were invariably encountered at operation in one frontal lobe. The seizures were somatomotor, generalized grand mal, and had been treated with anticonvulsants previous to admission to our service.

A history of unsteadiness in walking was elicited in the 4 cases of cerebellar lesions.

Signs of increased intracranial pressure were present in all cases. The criteria used for increased intracranial pressure were (a) papilledema and (b) x-ray evidence of widening of the cranial sutures in children and of erosion of the clinoid processes of the sella turcica in adults. Papilledema was usually severe, fluctuating between 3 and 6 diopters. It was associated with subhyaloid hemorrhages in 6 cases and with secondary optic atrophy and marked loss of vision in 3. There were no significant variations in the peripheral or central visual fields.

Involvement of other cranial nerves was unusual. The 6th, 7th, and 8th on the right were affected in Case 3, which with ipsilateral cerebellar signs led us to make a diagnosis of cerebellopontile tumor: at operation a tuberculoma of the right cerebellar lobe with projection into the cerebellopontile recess was disclosed. The other patient in whom cranial nerve involvement was found was Case 8, who showed a bilateral 6th nerve palsy, an absent left corneal, and a left peripheral facial with ipsilateral cerebellar signs and bilateral exaggeration of the deep reflexes. The diagnosis of an intrapontile glioma was made but at autopsy a huge tuberculoma involving the left cerebellum, pons, midbrain, cerebral peduncle and thalamus was found.

Contralateral hemiplegia was found in 4 patients with frontal lobe lesions (Cases 1, 2, 7 and 10). Ipsilateral cerebellar signs were present in all cases of cerebellar tuberculomas (Cases 3, 6 and 9) and in Case 8.

(b) *Epidural.* In the 1 case in this group the only symptom was a continuous dull pain localized over the right parietal region with occasional episodes of acute exacerbation. Exquisite tenderness over the right parietal bone, near the vertex, was the only positive sign. Plain x-rays of the skull revealed an irregular area of erosion in the right parietal bone, about the size of half a dollar, which was interpreted by the roentgenologist as a metastatic carcinoma. At operation an epidural tuberculoma was disclosed.

DIAGNOSIS

In the cases under discussion the preoperative diagnosis of tuberculoma was made in 2: in Case 3, who gave a history of tuberculous contact in the family, and in Case 9, whose chest x-rays showed a small parenchymatous lesion in the left pulmonary base. In 7 of the cases the diagnosis of brain tumor was made and in 1 a brain abscess was suspected.

There was no x-ray evidence of calcification of the lesions in any of our cases. The only roentgenological abnormalities were those produced by intracranial hypertension, namely, marked separation of the sutures in children and erosion of the sella turcica or its processes in adults. Ventriculography was performed in all the cases of intracerebral tuberculomas and by this diagnostic aid their location was disclosed in every instance.

Tuberculin intradermal tests were done in 3 of the 5 children: a positive reaction was obtained in every instance.

The final burden of proof in the diagnosis of intracranial tuberculomas in our series lay on the histological verification of the lesions. As a whole,

a diagnosis of tuberculoma can not be made preoperatively, although one may suspect its presence. A tentative diagnosis may be entertained when there is an extracranial tuberculous focus, a history of contact with tuberculous individuals, or when signs of increased intracranial pressure are present during the course of or after an apparent clinical cure of tuberculous meningitis. In this last respect I may say that during the past 3 years we have been called in consultation by our local Children's Hospital in 25 cases of tuberculous meningitis with signs of increased intracranial pressure. All these patients showed internal communicating hydrocephalus which at autopsy was found to be caused by obstruction of the cisterns at the base; no evidence of tuberculomas, gross or microscopic, could be disclosed in any of them.

In any event, I repeat, if the diagnosis of tuberculoma is made preoperatively, a conclusive and certain proof can not be obtained, even in the presence of extracranial tuberculosis, until the histological study of the lesion has been undertaken, as any true cerebral neoplasm may coexist with tuberculosis elsewhere.

TABLE 2

Location and weight of tuberculomas

Case No.	Intracerebral	Epidural	Weight (gm.)
1	Left frontal		19.0
2	Right frontal		112.5
3	Right cerebellar		16.0
4	Left temporal		46.0
5		Right parietal	10.0
6	Right cerebellar		27.0
7	Right frontal		68.5
8	Left cerebelloponto-mesencephalothalamic		?
9	Right cerebellar		38.0
10	Right frontal		14.0

LOCATION AND WEIGHT OF THE LESIONS

In 9 cases the lesion was solitary. In Case 7 there were two tuberculomas: one disclosed and removed at operation and one found at autopsy. As has already been mentioned, there were 1 epidural, located over the right parietal region, and 9 intracerebral tuberculomas. Among the intracerebral lesions (Figs. 1 and 2) 3 were located in the right cerebellar lobe, 3 in the right frontal and 1 each in the left frontal and left temporal lobes. Autopsy in Case 8 disclosed a tuberculoma which extended from the left cerebellar lobe to the left pons and midbrain, left cerebral peduncle and thalamus.

Nine tuberculomas were completely removed at operation. The epidural tuberculoma looked grossly like a nonspecific granuloma *en plaque* secondary to a destructive tuberculous lesion of the parietal bone. It was adherent to the dura, showed no subdural or intracerebral invasion and had a total weight

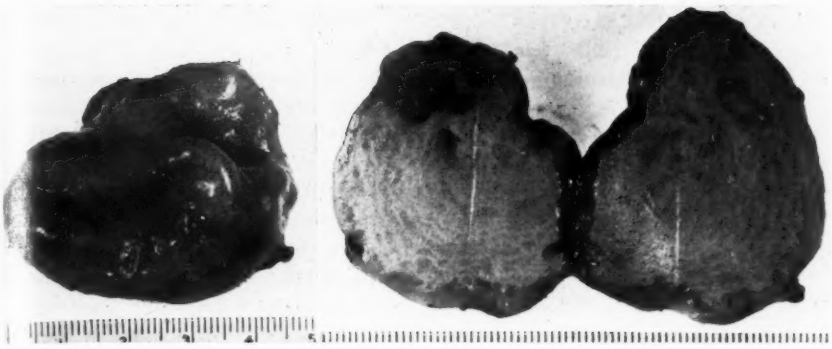

FIG. 1

o: 10 gm. The 8 intracerebral tuberculomas presented a uniform appearance: all of them projected into the brain substance, just a small area appearing over the cortex, and only 3 were adherent to the inner surface of the overlying dura mater.

The color of the lesions varied from a dirty yellow to a reddish-gray. The consistency was hard. The neighboring cerebral or cerebellar cortices presented uniformly a widespread edema, unlike that encountered with

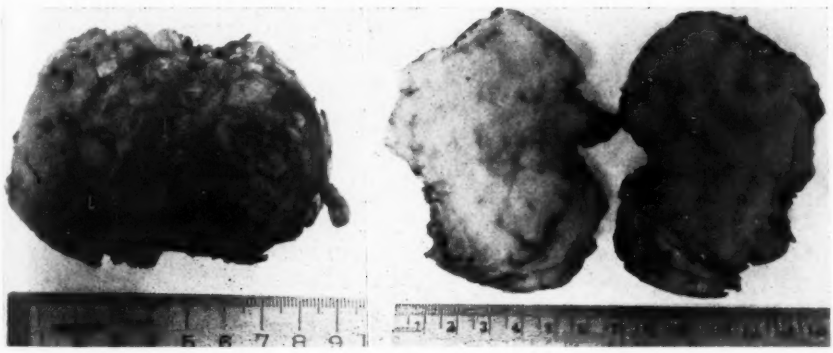

FIG. 2

gliomas and abscesses. This type of edema gave the neighboring convolutions a water-logged appearance, glassy-like, as if one could actually see through them, and it was so constant that a diagnosis of tuberculoma could be made invariably at the operating table upon opening the dura. The average weight of the tuberculomas was 43 gm., the smallest 14 gm., and the largest 112.5 gm. It is noteworthy that the patients with the largest tuberculomas (Cases 2 and 7) had a duration of symptoms of 24 and 36 months respectively.

COEXISTENCE WITH CLINICAL EVIDENCE OF EXTRACRANIAL TUBERCULOSIS

Among these cases there was only 1 in which a diagnosis of a suspicious extracranial active focus could be made. This was Case 9, in which the roentgenologist diagnosed a well-defined parenchymatous lesion in the left pulmonary base which cleared up completely after operation with the administration of streptomycin and paraaminosalicylic acid. Three patients died postoperatively and no gross evidence of extracranial tuberculosis was found at autopsy. This, however, does not mean that an active focus was not present as serial sections of the tracheobronchial and mesenteric lymph nodes were not made. Of these 3 patients, only 2 received adequate streptomycin therapy.

TREATMENT

All 10 patients were operated upon. An immediate postoperative diagnosis of tuberculoma was made in 9 cases. In Case 8 the diagnosis of an intrapontile glioma with invasion to the left cerebellopontile recess was made but no tumor at the angle was disclosed through a left suboccipital craniectomy. The autopsy findings are discussed elsewhere in this paper. This particular patient was subjected to intensive deep x-ray therapy, e.g., 10,000 r.u. postoperatively, but died 3 months later from the effects of intracranial hypertension.

As already mentioned, a complete extirpation of the lesion was performed in 9 cases. In the treatment of the intracerebral tuberculomas particular emphasis was placed on resecting about 1.5 cm. of uninvolved cerebral tissue at the edges. Frozen sections were made as we proceeded with the operative closure and as soon as the diagnosis of tuberculoma was established, dihydrostreptomycin, 0.50 gm., was given intramuscularly and 0.050 gm. intrathecally by the lumbar route while the patient was on the operating table. The intrathecal streptomycin was continued every other day for a total of 3 doses. The subsequent treatment in every case, regardless of the patient's age, consisted of dihydrostreptomycin, 0.50 gm., intramuscularly twice a day for 1 month and 0.50 gm. intramuscularly daily for 6 additional weeks. Case 9 received in addition paraaminosalicylic acid for the first 6 weeks postoperatively. Cases 2 and 7 showed evidence of tuberculous meningitis on the 29th and 48th postoperative day respectively. These two patients were given dihydrostreptomycin, 0.050 gm., intrathecally every other day in addition to 0.50 gm. intramuscularly twice a day until their time of death. Promin, 5.0 gm. intravenously, was given daily for 4 weeks to Case 2. General supportive measures were administered in every instance.

No permanent sequelae from the use of dihydrostreptomycin were noticed in any of the 7 survivors. In Case 1 dihydrostreptomycin, 0.50 gm., was given intrathecally by mistake on the 2nd postoperative day. Fifteen minutes after its administration the child became deeply unconscious, with dilated and fixed pupils, absent corneal and deep reflexes, and urinary reten-

TABLE 3

Treatment and end results

Case No.	Operation	Streptomycin	PAS	Promin	Follow-up	End Result
1	Craniotomy Complete removal	Yes	No	No	36 mos.	Good
2	Craniotomy Complete removal	Yes	No	Yes	3 mos.	Died. Tbc. meningitis
3	Craniectomy Complete removal	Yes	No	No	36 mos.	Good
4	Craniotomy Complete removal	Yes	No	No	36 mos.	Good
5	Craniectomy Complete removal	Yes	No	No	24 mos.	Good
6	Craniectomy Complete removal	Yes	No	No	18 mos.	Good
7	Craniotomy Complete removal	Yes	No	No	3.5 mos.	Died. Tuberculoma, left temporal
8	Craniectomy, exploratory	No	No	No	3.5 mos.	Died from hydrocephalus
9	Craniectomy Complete removal	Yes	Yes	No	16 mos.	Good
10	Craniotomy Complete removal	Yes	No	No	12 mos.	Good

tion, and he was irresponsive even to painful stimuli. His respirations were 8 per min. and his pulse rate was 48. Supportive measures were instituted. The child recovered consciousness 72 hours later and made an ultimate recovery without sequelae.

END RESULTS

There were 3 deaths and 7 survivals in our small series of cases. The postoperative deaths will be analyzed under a separate heading. The 7 survivors have been followed periodically from 12 to 36 months and all are living and well up to the time of this communication. Cases 1, 3 and 4 are in good health after 36 months. Cases 5, 6, 9 and 10 are living and well after 24, 18, 16 and 12 months respectively. No clinical evidence of extracranial tuberculosis has been disclosed in any of these patients during the specified periods of time. The children included in this series are among the survivors.

ANALYSIS OF POSTOPERATIVE DEATHS

The 3 patients who died were adults. In Case 8 the true nature of the lesion was discovered at autopsy which showed, as already mentioned, a sausage-shaped tuberculoma which extended from the left cerebellar lobe to left pons, midbrain, cerebral peduncle and thalamus. The cisternae pontis and interpeduncularis were occluded by the tumor. If the true nature of the growth had been established at operation, a decompressive measure to relieve the hydrocephalus combined with streptomycin therapy, could possibly have given this patient a better chance for survival.

The other postoperative deaths occurred in Cases 2 and 7 from tuberculous meningitis. Both patients were given dihydrostreptomycin, and Case 2 received in addition intravenous Promin. Case 2 showed evidence of tuberculous meningitis on the 29th and died on the 87th postoperative day. Autopsy confirmed the diagnosis of tuberculous meningitis. In Case 7 meningitis developed 48 days and death occurred 101 days after operation. Autopsy showed in addition to the tuberculous meningitis, a tuberculoma in the left temporal lobe, 3.5 cm. in diameter. Because of signs of increased intracranial pressure on the 50th postoperative day, ventriculography had been performed, which showed only an internal hydrocephalus without evidence of a supratentorial space-occupying lesion.

There are certain common features in these 2 cases. Both patients were Indians, and had had the longest duration of symptoms. Both came into the hospital hemiplegic and in extreme emaciation. The intracranial pressure was so great and the loss of vision so advanced that in order to preserve vision and life we had to operate upon them within the first 24 hours following admission. And finally, both of these patients had the largest tumors. In Case 7 it is conceivable that the meningitis might have come from the additional tuberculoma while in Case 2 it was a direct sequela of the operative procedure. Case 7 has demonstrated the futility of using streptomycin alone in the treatment of intracranial tuberculomas.

CONCLUSIONS

From the presentation of these cases we may draw the following conclusions:

1. Tuberculomas are among the common intracranial expanding lesions.
2. They are more prevalent in the first two decades of life.
3. The duration of symptoms may fluctuate from 2 to 36 months.
4. A history of fever may be obtained at the onset of symptoms.
5. Headaches and early signs of increased intracranial pressure are the most constant clinical features.
6. The water-logged, glassy appearance of the surrounding brain may help in the gross diagnosis of the lesion at the operating table.
7. A definite diagnosis can not be made until the histological examination of the lesion is undertaken.
8. A complete surgical removal of these lesions, whenever feasible, combined with adequate streptomycin therapy should be the method of choice in their management.
9. Children seem to have a better chance of survival than adults.

SUMMARY

1. Our experience in the surgical treatment of 10 consecutive cases of intracranial tuberculomas has been presented.

2. Their incidence, symptomatology, operative findings and end results are discussed.

3. Complete surgical extirpation with adequate streptomycin therapy was performed in 9 cases.

4. Of these 9 patients, 2 died from tuberculous meningitis and 7 are living and well for a period ranging between 12 and 36 months.

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HYPERTROPHIC SPINAL PACHYMENINGITIS

WITH SPECIAL REFERENCE TO APPROPRIATE SURGICAL TREATMENT*

PAUL C. BUCY, M.D., AND L. WILLARD FREEMAN, M.D.†

Department of Neurology and Neurological Surgery, University of Illinois College of Medicine, and The Chicago Memorial Hospital, Chicago, Illinois

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CHARCOT and his pupil Joffroy studied and delineated the clinical picture of hypertrophic pachymeningitis of the cervical spinal canal so accurately that little has been added to our knowledge since then. In 1869 they described a case in the Archives de Physiologie[6] and in 1871 Pierret[24] reported another example from the service of Charcot. In 1873 Joffroy[13] published his classical thesis on the subject under Charcot's direction. They were able to find only 4 cases of this condition that had previously been recognized and reported. The first example was recorded by Abercrombie[1] and the second by Ollivier d'Angers.[23] William Gull[8] in 1858 published the third case, with illustrations of the appearance of the cross-section of the thickened dura mater and the compressed cervical spinal cord. They credited Köhler with a fourth case but review of Köhler's original description[15] reveals that it was the pia and arachnoid that were grown together forming a thick, leather-like covering to the spinal cord and that the dura mater was not involved in this process.

Charcot and Joffroy pointed out that the symptomatology is divisible into three periods. (1) *The painful period.* The onset is with pain in the neck and back of the head, which soon begins to radiate into the upper extremities. These pains are caused by involvement of the cervical meninges and, in turn, of the posterior cervical spinal roots. At first the pain is remittent but after 2 to 5 months it becomes continuous. It is often associated with stiffness of the neck and is aggravated by movement of the neck. Finally, tingling, like needles and pins, develops in the hands and fingers, and sensibility in the upper extremities is gradually impaired. (2) *Atrophic paralysis.* The painful period and that of atrophic paralysis in the upper extremities may be combined or clearly separated. In any event the pain occurs first and after a variable interval atrophy and weakness appear in the upper extremities. The distribution of the atrophy is variable. It may appear in one or both upper extremities. The small muscles of the hands are usually involved, but the muscles of the arms are by no means spared. (3) *Spastic paralysis.* As the disease progresses a spastic paralysis of the lower extremities, with the usual changes in reflexes, appears. Respiratory movements may be interfered with. The bladder and bowels are usually affected and sensory

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† Now at The University of Indiana College of Medicine, Indianapolis.

changes of variable nature and extent develop. Eventually a severe paraplegia supervenes and the patient becomes bedridden with paroxysmal flexor-defense reflexes.

Charcot and Joffroy recognized that the dura mater posterior to the spinal cord was most severely involved and that the disease usually occurred in the cervical region. They were also aware that it might occur in other parts of the spinal canal and might even involve the intracranial dura mater, particularly that in the posterior fossa. In the latter location the disease might give rise to paralysis of various cranial nerves. They described the thickened dura mater as composed of concentric layers of fibrous connective tissue, similar to the cornea, the vessels increased in number and their walls thickened. They believed that the disease initially is confined to the dura mater but that gradually the spinal roots become inflamed and compressed, and that the involvement tends to extend gradually to the leptomeninges and even to the spinal cord. They noted that the leptomeninges often become thickened and that the dura mater may become adherent to them and to the spinal cord. In addition to evidence of inflammation the spinal cord may develop areas of softening and cavitation secondary to the prolonged and increasing compression.

They clearly distinguished between hypertrophic pachymeningitis and various other diseases of the dura mater. They were well aware of the difference between this condition and hemorrhagic pachymeningitis interna (subdural hematoma), which they frequently found intracranially but seldom intraspinally; between it and pachymeningitis externa which was seen particularly in association with Pott's tuberculosis of the vertebrae; and between it and purulent affections of the internal surface of the dura mater. They also stated clearly that they had been unable to find the cause for hypertrophic pachymeningitis, and that no specific or satisfactory form of treatment had been found.

Since the 1870's little progress has been made and much confusion has been added. The distinct entity that Charcot and Joffroy so clearly described has been largely lost sight of in a welter of confusion with epidural and subdural disorders, particularly epidural granulomas and intradural inflammatory processes secondary to the acute meningitides. Probably the most serious misunderstanding has come from the now nearly universally accepted belief that the disease is almost invariably of luetic origin. This is simply not true. The disease has also occasionally been erroneously attributed to tuberculosis. It would not be possible to state that these infections had never given rise to hypertrophic spinal pachymeningitis but when one reviews the cases so diagnosed he finds that they either occurred before the introduction of the Wassermann reaction (1906) and the discovery of the Treponema pallidum (1905) or rested solely upon the microscopic evidence of a chronic inflammatory process in the dura mater without any positive evidence as to the etiology. In fact in many cases the disease has been attributed to syphilis in spite of negative serological tests on the blood and

spinal fluid and in the absence of any other evidence of syphilis. Joffroy stated very frankly that the etiology was unknown and that the long list of possible causes that had been suggested, including arthritic diathesis and living in a cold damp place, had not been substantiated. It is important to recognize that we are still ignorant of the causative agent and that valuable time should not be lost in administering antiluetic treatment in the absence of positive evidence of syphilis. Nor should surgery be unduly delayed in those occasional cases with evidence of syphilis as even here antiluetic therapy may prove ineffective while proper surgical treatment may bring about improvement.[25] It must be borne in mind that with progression of the disease, the dura mater may become densely adherent to the leptomeninges and the spinal cord making satisfactory separation impossible or very difficult and that eventually changes within the spinal cord, softenings and cystic degeneration, may become irremediable.

The first operation for this disease, according to Kment and Salus,[14] was performed by Schede in 1901 (reported by Schultze[28]). Since then a number of patients with this condition have been operated upon. In 1931, Kment and Salus reported 3 cases of their own and 16 others that they had been able to find in the literature. Of these 19 patients, 12 were improved or cured. However, as some had been observed for only a short time after operation, often only a few months, no final conclusion as to the results can be drawn from these cases. Furthermore, in some of the cases the disorders were not hypertrophic pachymeningitis of the type described by Joffroy and Charcot, but were instances of slight thickening of the dura mater (2 or 3 mm.) in reaction to an extradural or intradural inflammatory process (e.g. Case 1 of Kment and Salus[14]), or, as in the case of Odin and Runström,[21] were examples of chronic leptomeningitis, not pachymeningitis.

The operations that have been performed have varied from mere incision of the dura mater, to separation of the dura mater from the leptomeninges and spinal cord, and finally to actual extirpation of the involved dura mater. This latter procedure was apparently first recommended but not done by Borchardt[3] in 1912. This extensive procedure is the most logical and has given the best results, although on occasion mere incision of the dura mater has been sufficient to result in marked improvement (Hohlbaum, Case 1;[11,12] Ricard, Dechaume and Croizat;[27] García Díaz and Buylla[7]).

For over 8 years we have followed the 2 patients we operated upon for this condition. In both of these that portion of the greatly thickened dura mater that lay posterior to the emergence of the spinal roots was removed and the complete recovery that followed the operations has been maintained.

Case 1. #85165. Female, aged 53 years.

Summary. Sharp shooting pains in shoulders and arms, 3 months. Paralysis of right leg, 10 days. Inability to urinate, 3 days. Diminution of sensation below T3; weakness of arms and left leg; total paralysis of right lower extremity; atrophy of muscles of both hands; hyperactive tendon reflexes throughout; absent abdominal

reflexes; bilateral Babinski sign. Negative Wassermann and Kahn tests on blood and CSF. No cells in spinal fluid; total protein 1330 mg. per cent. Colloidal gold curve 0013455555. Obstruction of spinal canal to pantopaque above T2. Laminectomy C3-T2. Grossly thickened dura mater excised. Dramatic postoperative recovery. Continued good health.

History. A.P., a housewife 53 years of age, was referred by Dr. Marie Ortmayer of Chicago and admitted to The Chicago Memorial Hospital on Feb. 23, 1944. For several months she had noted numbness and tingling in both arms to a minor degree but since Dec. 15, 1943 she had suffered from sharp shooting pains which began in the right shoulder and radiated down the right arm. These pains soon spread to the left shoulder and arm. They were very severe and frequently incapacitated her completely. Ten days prior to admission the right leg became weak and she soon became unable to use it. During the last 3 days she had had no urge to urinate and was unable to do so. She had been catheterized repeatedly.

FIG. 1. *Case 1.* Pantopaque myelogram showing complete obstruction at the 1st thoracic vertebra.

Examination. The cranial nerves were intact. There was diminution of perception of pin prick and light touch below the 3rd thoracic segment, more marked on the right side. Vibratory sense was intact but there was slight diminution in position sense in the toes of both feet. The localization of points stimulated was not accurate on the abdomen or the right lower extremity and the perception of figures written on the skin was totally inaccurate on the legs but good on the palms. There was moderate atrophy of the small muscles of both hands. Both arms were weak, particularly the right. The left leg was fairly strong but the right leg was totally paralyzed. No fibrillations were seen. The tendon reflexes were hyperactive in the arms and legs. The abdominal reflexes were absent. Babinski's sign and all of the supporting signs were positive bilaterally. The neck was not stiff.

Urinalysis was negative. Examination of the blood revealed an anemia of 3,890,000 RBC/c.mm., 12.6 gm. per cent Hb., 7,100 WBC/c.mm., and negative Wassermann and Kahn tests. The spinal fluid contained no WBC; total protein was 1330 mg. per cent; Wassermann's test was negative and colloidal gold curve was 0013455555.

Pantopaque was injected into the spinal canal and its course observed under the fluoroscope as the patient was tilted head downward. Its flow was completely obstructed at the level of the interspace between the 1st and 2nd thoracic vertebrae (Fig. 1). Roentgenograms of the upper thoracic spine showed a slight scoliosis with the concavity toward the right side. Except for some osteo-arthritic changes of the

5th, 6th and 7th cervical vertebrae the bony structure appeared normal. The intervertebral disc between the 6th and 7th cervical vertebrae was narrowed. There was no abnormality of any of the pedicles.

Operation. On Feb. 25, 1944, a laminectomy from the 3rd cervical through the 2nd thoracic vertebra was done. The dura mater was pinkish-grey in color, gelatinous in appearance and grossly thickened. The thickening of the dura mater extended from the upper border of the 3rd cervical to the upper border of the 2nd thoracic vertebra (Fig. 2). The dura mater was excised in two strips measuring 9 cm. in

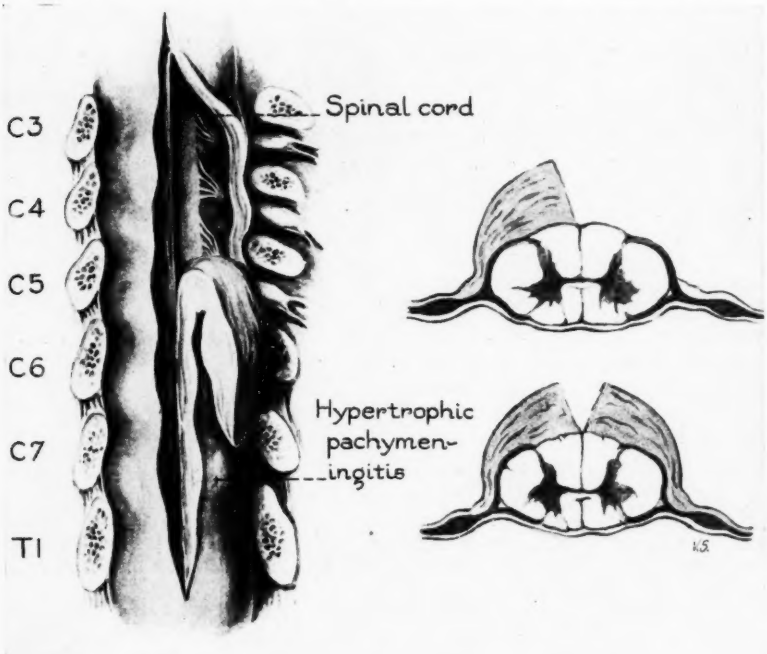

FIG. 2. *Case 1.* Artist's sketch of operative findings. The thickened dura mater was removed in two strips. The cross section views at the right show the extent of the extirpation down to the point of exit of the spinal nerves and the relation of the dural thickening to the posterior part of the spinal cord.

length, and 2 cm. in width; they were 1 cm. thick at the greatest point. The excision extended laterally and forward to the point of emergence of the spinal roots from the dural sac. The greatest thickening lay posterior to the spinal cord but the portion of the dura mater that extended anterior to the spinal nerves was also somewhat involved. The spinal cord appeared to be flattened and moderately indented at several points. The dura mater was not adherent to it. There was considerable troublesome oozing of blood from the cut edge of the dura mater. This was finally controlled and the wound was closed tightly.

Bacteriological Studies. Cultures of the tissue removed proved sterile and tissue injected into guinea pigs gave negative results.

Microscopic Examination. Sections of the abnormal dura mater (Fig. 3) were

composed of dense fibrous tissue heavily infiltrated with lymphocytes and plasma cells intermingled with numerous giant cells of foreign body type. These giant cells varied widely in size but usually contained numerous hyperchromatic nuclei situated at the periphery of the cytoplasm (Fig. 4). There were also fairly well circumscribed accumulations of lymphocytes (Fig. 5) with centrally located giant cells. No necrosis was seen. Although a special search was made, after staining sections with various methods, no organisms of any kind could be found. Sections of the bone of the spinous processes and laminae revealed a few more plasma cells than are usually seen in

FIG. 3. *Case 1.* Photomicrograph of hypertrophic dura mater. There are scattered accumulations of inflammatory cells among the fibers of the dura mater. Hematoxylin and eosin, ×45.

the bone marrow but no definite abnormality. Both Dr. Otto Saphir and Dr. Percival Bailey regarded this as a granulomatous hypertrophic pachymeningitis of unknown etiology.

Postoperative Course. The patient improved rapidly and was discharged from the hospital on March 18, 1944. She was able to walk and showed more strength in her hands. However, she continued to complain of pains in her neck and shoulders although they were not so severe or incapacitating as they had been before operation. In view of the apparently favorable effect of X-ray therapy in Case 2 (reported below) she was given similar treatment to the cervical area and received 3,250 r., divided into 26 treatments given between April 27 and June 8, 1944. The pains soon subsided. She has been followed at frequent intervals since and was last seen in the

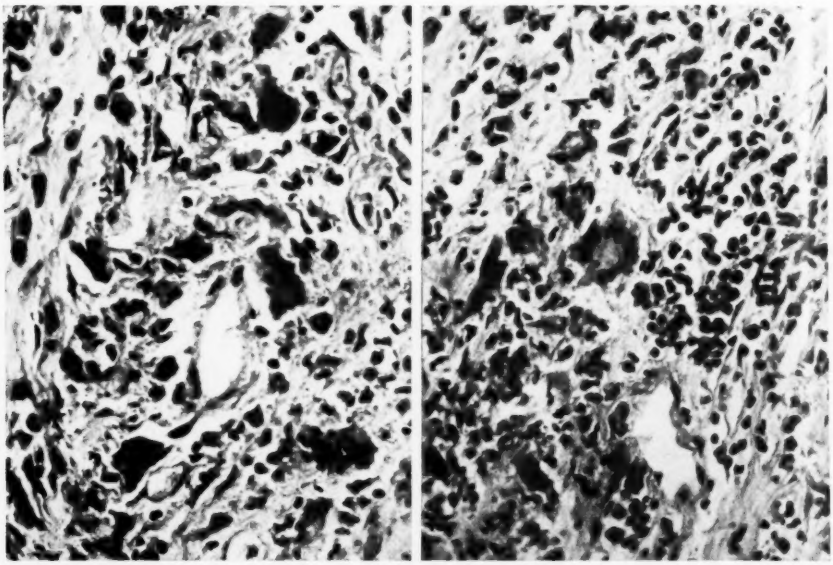

FIG. 4. *Case 1.* Multinucleated giant cells, lymphocytes and plasma cells are scattered throughout the thickened dura mater. *Left,* ×365. *Right,* ×325.

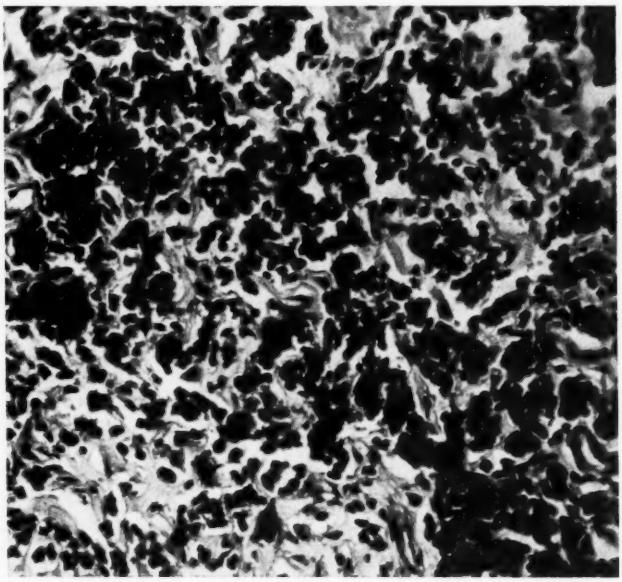

FIG. 5. *Case 1.* In one region a dense infiltration of lymphocytes was found. ×340.

Spring of 1951. She is perfectly well. The atrophy of the small muscles of the hands has completely disappeared. There is no weakness anywhere nor are there any sensory changes.

Comment. This is a typical example of hypertrophic pachymeningitis of the dura mater in the cervical region. It presents all of the clinical findings that Charcot and Joffroy[6] described. However, the course was shorter than in their cases or in our Case 2. The prompt recovery of the right leg from a complete paralysis could hardly have been more dramatic.

Whether the subsidence of the radicular pains was aided by the radiation therapy is of course debatable and cannot be solved by either of our 2 cases. Such a possibility is strongly suggested.

Case 2 closely resembles Case 1 except that there was a longer history of pain and discomfort in the area supplied by the involved posterior roots and hypertrophy of the dura mater was in the upper thoracic region.

Case 2. #83629. Male, aged 52 years.

Summary. Intermittent pain in upper back and shoulders, 3 years. Shock-like pain down spine on coughing 1 year. Numbness of trunk and legs, difficulty with bowel and bladder and with walking, 2 to 3 weeks. Sensory loss below T5; spastic paraparesis. Negative Wassermann and Kahn tests on blood and CSF. Complete spinal block; xanthochromic CSF; protein 720 mg. per cent. Laminectomy C7-T5. Hypertrophic granulomatous pachymeningitis; thickened dura mater excised. Practically complete recovery.

History. A.E., a hod carrier 52 years of age, was referred by Dr. M. L. Weinstein of Chicago and was admitted to The Chicago Memorial Hospital on Nov. 14, 1943. The patient had been born in Italy.

For 3 years he had suffered from burning pains and a sense of constriction in his upper back and shoulders. At times he had been free of pain. For 1 year coughing had caused an electric-shock-like pain to radiate down his spine from his upper back. For the last 2 weeks there had been numbness of his body from the upper chest downward, and urinary frequency with trouble in voiding. He had had difficulty in defecating and fecal incontinence for 4 days. During the 3 weeks prior to admission the pain had been constant and severe. His legs had become weak, with increasing difficulty in walking. Finally, he was confined to bed.

A benign chondroma had been removed from the right thumb in 1941. He had had gonorrhea in 1918, influenza in 1920, and a peritonsillar abscess in 1930. He consumed a moderate amount of alcohol and became intoxicated about once a month. He was married. His wife was living and well, and they had four normal children. There had been no miscarriages.

Examination. General physical findings were negative except that the rectal sphincter was completely relaxed, the prostate gland was moderately enlarged and there was a hard immovable mass, 1×2 cm., on his right thumb under an old scar.

Neurological examination disclosed an analgesia and hypesthesia below the level of the 5th thoracic segment, and absence of sense of position in the toes and of vibratory sensibility from the anterior superior iliac spines downward. The cranial nerves were intact. Strength in the arms was normal but there was marked weakness in the legs, greater in the left. There was an increase of resistance to passive manipula-

tion of the legs but not of the arms. The tendon reflexes in the arms were normally active while the knee and ankle jerks were hyperactive. Sustained clonus was present at both ankles. Babinski's sign and all of the supporting signs were positive. There was no stiffness of the neck and no tenderness of the spine. His gait was hesitant and "bouncing", and he had marked difficulty in walking.

Urinalysis and blood count were normal. Wassermann and Kahn tests on blood were negative. Total protein of blood serum was 6.7 gm. per cent with 3.7 gm. albumen and 3.1 gm. globulin. Gastric analysis revealed no free hydrochloric acid.

X-ray examination of the cervical and upper dorsal spine revealed no change except that the right pedicles of the 4th and 5th thoracic vertebrae were not as sharply defined as the others. Roentgenograms of the chest showed only pleural thickening at the base on the left side and a marked convexity of the right border of the ascending aorta.

On lumbar puncture the initial pressure was 165 mm. of fluid. This pressure was not altered by compression of the veins in the neck, but abdominal compression caused a rise to 210 mm. The fluid was very xanthochromic; it contained no cells; Pandy's test was very strongly positive; protein was 720 mg. per cent; Wassermann and Kahn tests were negative. The colloidal gold curve was 0000002331.

Operation. On Nov. 18, 1943 a laminectomy of the 7th cervical through the 5th thoracic vertebra was made. The ligamenta flava were directly adherent to the dura

FIG. 6. *Case 2.* Photomicrograph of hypertrophic dura mater. Clusters of inflammatory cells are scattered among the fibers of collagen of the dura mater. Hematoxylin and eosin, ×45.

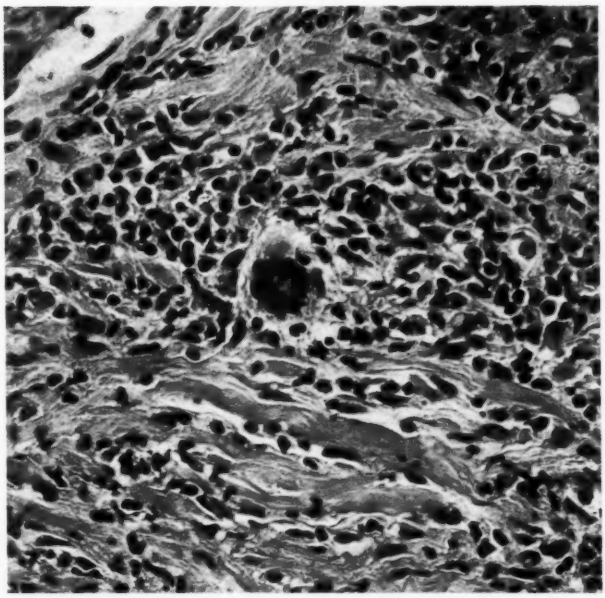

FIG. 7. *Case 2.* Multinucleated giant cells, lymphocytes, plasma cells, and histiocytes among the coarse fibers of collagen. ×350.

mater. There was no epidural fat present. The dura mater was greatly thickened and filled the spinal canal. On its posterior surface could be seen indentations where the laminae had pressed against it, and it had bulged posteriorly between them. The greatest thickening was at the level of the 3rd and 4th thoracic vertebrae. The dura mater was first incised in the midline but was too thick and stiff to be reflected laterally to expose the spinal cord. It therefore was excised in two pieces. On each side the excision extended from the midline to the point of exit of the spinal nerves from the dural theca. The dura mater was not adherent to the leptomeninx. There was little if any thickening of the dura mater above the 7th cervical vertebra or below the 5th thoracic, or anterior to the points of emergence of the spinal nerves. The tissue removed measured 1.2 cm. in thickness, 2.0 cm. in width and 7.5 cm. in length in greatest dimensions. Its inner surface was smooth, glistening and greyish in color with numerous vessels visible in it. The spinal cord and nerve roots were obviously compressed but not otherwise abnormal. The wound was closed tightly.

Microscopic Examination. Sections of the material removed (Fig. 6) consisted of much hyalinized connective tissue richly infiltrated with lymphocytes, endothelial leucocytes and plasma cells as well as fibroblastic cells (Fig. 7). In addition to this diffuse infiltration there were more or less well localized groups of similar cells, mostly lymphocytes or plasma cells (Fig. 8). In these circumscribed areas were a number of giant cells some of which appeared to be of the Langhans type while others had centrally placed overlapping nuclei. In none of these foci was there any predominance of endothelial leucocytes. A careful search with special stains for infectious organisms, inclusion bodies or yeast-like structures yielded negative results. The

blood vessels showed thickened walls but no endarteritic or periarteritic changes. There was no necrosis.

In the opinion of our pathologist, Dr. Otto Saphir, these sections gave no evidence of leukemic infiltration, neoplasm, syphilis or tuberculosis. He referred to this as a granulomatous hypertrophic pachymeningitis of unknown etiology.

Postoperative Course. The patient's recovery was rather slow but progressed steadily, so that he was discharged on Dec. 13, 1943. For a time after leaving the hospital he complained of pains in his shoulders and back. A course of X-ray therapy of unknown amount (1 treatment a week for 9 months) was administered by the referring physician, Dr. M. L. Weinstein, and shortly thereafter these pains subsided. He gradually recovered full control of his legs, bowel and bladder.

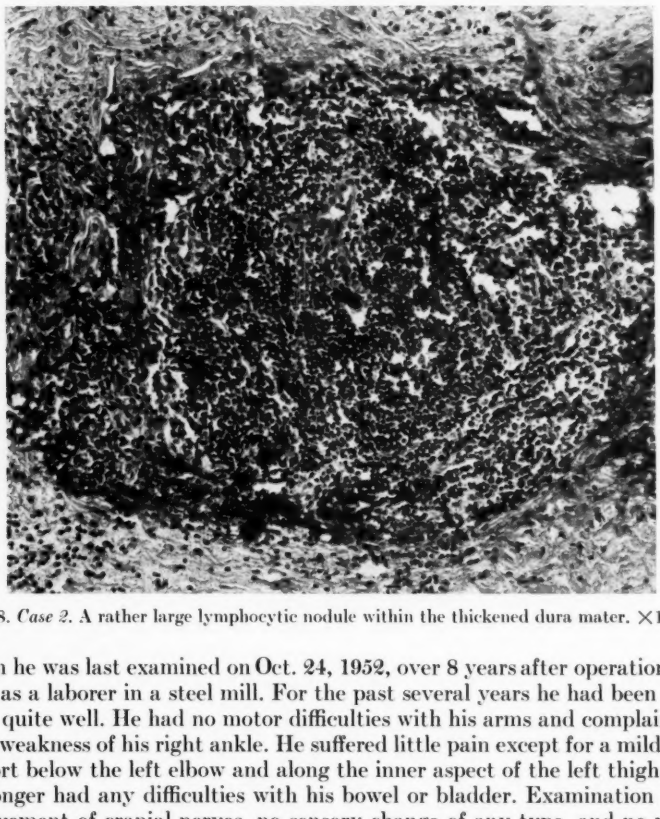

FIG. 8. *Case 2.* A rather large lymphocytic nodule within the thickened dura mater. ×125.

When he was last examined on Oct. 24, 1952, over 8 years after operation, he was working as a laborer in a steel mill. For the past several years he had been very active and quite well. He had no motor difficulties with his arms and complained only of slight weakness of his right ankle. He suffered little pain except for a mild burning discomfort below the left elbow and along the inner aspect of the left thigh and leg. He no longer had any difficulties with his bowel or bladder. Examination revealed no involvement of cranial nerves, no sensory change of any type, and no muscular weakness or atrophy. All tendon reflexes in both upper and lower extremities were definitely hyperactive. Those in the arms were equal whereas those in the right lower extremity were a little more active than those in the left. Babinski's sign was elicited on the right side. As he walked he tended to favor his right leg slightly and was not able to hop well on either foot alone. To all intents however, he had made a complete recovery from his previously completely incapacitating disability.

Comment. This seems to be a typical example of hypertrophic pachymeningitis of undetermined etiology. It differs from the usual cervical variety only in that it was located in the upper thoracic region. Clinically it presented the typical first stage of posterior-root irritation with radicular pain, followed after some 3 years by signs of compression of the spinal cord. The evidence of involvement of the anterior motor roots, localized atrophic muscular atrophy, which is such a common manifestation of the cervical form of this disease, was overlooked if it was present in this case. This is probably accounted for by such changes being much less apparent with involvement of the upper thoracic anterior roots.

DISCUSSION

Etiology. It is noteworthy that neither of these 2 patients had any evidence of a syphilitic infection, nor were we able to establish the nature of the infectious agent although the condition appeared to be the result of some low-grade chronic inflammatory process. A number of observers have reported the occurrence of an abnormal colloidal gold curve with hypertrophic pachymeningitis, whether intracranial or spinal in location, even when there were no other evidences of syphilis (Hassin and Zeitlin[10]—5543211000 and 4555543210; Naffziger and Stern[20]—0012211000; Lewis, Hall and Bernstein[17]—5555554421). This, of course, is not surprising in view of the gross abnormality of the protein content of the cerebrospinal fluid that is so commonly present. However, in our Case 2 the curve was only slightly abnormal (0000002331) whereas in Case 1 it was grossly abnormal (0013455555). In these two instances the greatest change was in the right side of the curve. This is not typical and has not been the case in any considerable number of other reports.

The cases reported here are typical in their lack of evidence of syphilis. The idea that this condition is always or even commonly the result of syphilis is undoubtedly erroneous and has led to the extensive administration of useless antiluetic therapy and unfortunate delays in appropriate surgical treatment. On the other hand, it appears likely that on rare occasion hypertrophic pachymeningitis does arise as the result of syphilis.[25]

Pathology. The thickening, or hypertrophy, of the dura mater that occurs in these cases is characterized by a marked proliferation of collagenous fibers which are arranged in parallel rows and infiltrated with cells characteristic of a chronic inflammatory reaction. These are principally lymphocytes and plasma cells. There are also a variable number of gigantic polymorphonuclear cells. Some of these giant cells have their nuclei centrally placed and overlapping each other; others are of the foreign body type with the nuclei forming a ring at the periphery of the cytoplasm. Both types may be present in the same case. There are, in addition, foci in which there are accumulations of these various cells. There are, however, no areas of necrosis and no epithelioid cells. No infectious organisms of any kind can be demonstrated. There is usually an increase in the number of small blood vessels and a thickening of their walls. There is little or no tendency toward a perivascu-

lar arrangement of the inflammatory cells. Other authors have reported changes in the leptomeninges, the nerve roots and the central nervous system but there was no opportunity to make any observations on those tissues in our cases.

Localization. Our Case 1 is characteristic of the cervical form of this disease as originally described by Charcot and Joffroy. Undoubtedly this is the most common single locus for this unusual condition. However, in their original papers Charcot and Joffroy recognized that the same type of pathological change might be found elsewhere in the spinal canal and even in the intracranial cavity, particularly in the posterior fossa.

Case 2 is an instance of the same process occurring in the upper thoracic region. Although such a localization is uncommon a number of authors have recorded similar cases.[11,12,14,16,18,19,27–32] As one descends the spinal canal the incidence of this disease becomes less, but Ody[22] and Rendu[26] have each recorded instances of hypertrophic pachymeningitis at the thoracolumbar junction and Cassirer[4] found 1 case in which the disease involved the cauda equina. Involvement of the intracranial dura mater has been even less common than spinal involvement. Hassin[9] studied 2 cases with predominantly frontoparietal involvement, and Hassin and Zeitlin[10] made a detailed pathological study of a case in which the dura mater of the posterior fossa and above the tentorium as well as the tentorium itself was involved. Naffziger and Stern[20] reported a case in which the principal involvement was in the posterior fossa but the disorder did extend downward into the cervical spinal canal.

Symptomatology. There is little that one can add to the original description of Charcot and Joffroy. The disease is characterized by radicular pains referable to the site of the disease, muscular weakness and atrophy similarly localized, and muscular weakness and spasticity below the level of the compression of the spinal cord. The bowel and bladder are commonly involved. Changes in sensibility are also the rule. However, the changes are by no means characteristic of this disorder in contradistinction to any other compression of the spinal cord. Spinal (lumbar) puncture usually reveals the presence of an obstruction of the spinal subarachnoid space on Queckenstedt's maneuver. Where it has been used iodized oil has also demonstrated such an obstruction. It is to be anticipated that in an early case, perhaps during the period of radicular pain, an obstruction of the spinal subarachnoid space need not be present. The protein content of the spinal fluid is usually increased, often to rather high levels, with xanthochromia and, at times, coagulation of the fluid as Babonneix and Voisin[2] have pointed out. Furthermore, the colloidal gold curve is often grossly abnormal but it is in no way typical or diagnostic of the condition.

Treatment. As with intraspinal neoplasms there would seem to be only one form of treatment to be recommended, that is an extirpation of the growth that is compressing the spinal cord. As is shown by the cases presented, that form of treatment is highly satisfactory and not difficult to

accomplish. Naffziger and Stern[20] have shown the advisability of doing the same thing with similar intracranial lesions. It is not surprising, however, that even though the great bulk of the involved dura mater is excised the patient might continue to suffer from radicular pains. That was true in both of our cases. The spinal nerve roots at their points of emergence from the dural sheath are compressed by the hypertrophic dura mater. Furthermore, they are often involved by the inflammatory process. In both of our cases these pains gradually subsided and have largely or entirely disappeared. Whether the X-ray therapy which was administered postoperatively was influential in ameliorating these pains or whether they would gradually have subsided anyway is something we do not know. Nonetheless, we are convinced that with the severe compression of the spinal cord that is present in these cases, and with the ever-present danger of extension of the inflammatory process to the leptomeninx and to the spinal cord and of ultimate softening and necrosis of the spinal cord, it would be foolhardy to treat these patients only with the X-rays without first decompressing the spinal cord by removing as much of the involved dura mater as possible. It is also obvious that mere incision of the dura mater, with or without freeing it from the underlying leptomeninx and spinal cord, is inadequate surgical treatment.

SUMMARY

Two cases of hypertrophic spinal pachymeningitis, one in the cervical and one in the upper thoracic region, have been reported. Both patients were operated upon, and all of the grossly thickened dura mater lying posterior to the points of emergence of the spinal nerve roots was removed. Both made dramatic recoveries from severe spastic paraplegias. The recovery from the atrophic weakness of the upper extremities in the patient with a cervical lesion was also dramatic. In both instances the recoveries have been maintained for many years.

A study of these cases and of the literature reveals a rather constant clinical picture and the fact that there is no known etiological factor for this condition in the majority of cases. Specifically, this condition is seldom of syphilitic origin. There is no known form of useful treatment except the surgical excision of the hypertrophic dura mater that is compressing the nervous system.

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ORBITOFRONTAL LOBOTOMY

WITH REFERENCE TO EFFECTS ON 55 PSYCHOTIC PATIENTS*

JOHN R. GREEN, M.D.,† R. E. H. DUISBERG, M.D.,† AND
W. B. McGRATH, M.D.†

Neurosurgical Unit, Arizona State Hospital, Phoenix, Arizona

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THE undesirable effects of the standard frontal lobotomy operation are well known. They include changes of personality in respect to loss of social consciousness, ambition, imagination, and foresight, and a fairly low percentage of postoperative complications, including hemorrhage, infection, epilepsy and urinary incontinence.

Such therapy for certain abnormal mental states was introduced by Moniz‡[16] in Lisbon in 1935, by Freeman and Watts[9] in America in 1936, and modified by Lyerly,[14] McKissock,[15] and Poppen.[19] In attempts to improve these procedures, others have been substituted and include:

(1) Transorbital lobotomy, by Fiamberti[8] in 1937.
(2) Lower quadrant frontal lobotomy, by Hofstatter *et al.*[12] in 1945.
(3) Bilateral frontal gyrectomies, by Penfield[18] in 1947.
(4) Thalamotomy, by Spiegel *et al.*[23,24] in 1947.
(5) Undercutting of various portions of the premotor cortex, by Scoville[22] in 1949.
(6) "Topectomy" (the removal of Brodmann's areas 9 and 10), by Pool[6] in 1949.
(7) Isolation of the anterior cingulate area (Area 24), by Livingston[13] in 1951.

Our investigations concern selective frontal lobotomy of the orbitofrontal area in 55 chronically institutionalized mental patients, beginning on October 9, 1947. Orbitofrontal lobotomy was decided upon instead of the standard procedure for the following reasons: (1) to attempt to reduce the degree of blunting of the personality, and complications that follow the standard frontal lobotomy, (2) encouragement from the unconfirmed reports of Hofstatter and associates[12] in 1945, and (3) anatomic and physiologic evidence of concentration of frontothalamic projections in the orbitofrontal areas.

ANATOMICAL CONSIDERATIONS

One of the 3 primary divisions of the portion of the frontal lobes lying rostral to the precentral motor cortex (frontal, orbital, anterior cingulate), or subcortical connections of these divisions (dorsomedial and anterior

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† Professional Building, Phoenix, Arizona.

‡ The Nobel prize for 1949 in Medicine was awarded to Dr. Egas Moniz for original work in the field of psychosurgery.

nuclei of the thalamus and certain hypothalamic nuclei) are the areas of present-day psychosurgery. The major fronto-subcortical pathways affected by these procedures are diagrammed in Fig. 1.

Le Gros Clark[2] considers the dorsomedial nucleus of the thalamus as the primary relay station between the frontal lobes and the hypothalamus. It occupies the center of the thalamus and shows a point-to-point organization in its projection to circumscribed areas of the frontal cortex (Walker[27]). Thus, the main part of the nucleus (pars parvicellularis) projects as follows: (1) central part to frontal areas 9 and 10, (2) medial part to frontal areas 11 and 47, (3) dorsolateral part to frontal area 45 and (4) ventrolateral part to frontal area 8. The magnocellular part of the dorsomedial nucleus pro-

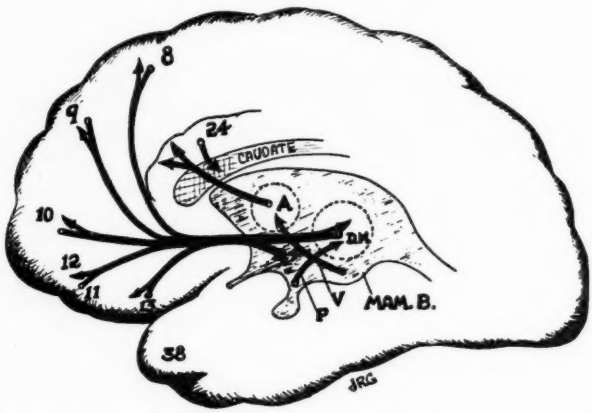


FIG. 1. Major fronto-subcortical pathways (Brodmann's cortical areas, orbital surface modified by Walker, redrawn from Le Gros Clark).

D.M. = Dorsomedial nucleus
A. = Anterior nucleus
MAM.B. = Mammillary body
V. = Bundle of Vicq d'Azyr
P. = Periventricular system, hypothalamus to D.M.

jects to orbital gyri (areas 13 and 14), and also receives connections from different parts of the hypothalamus (Le Gros Clark and Boggon[3]).

The anterior nucleus of the thalamus serves as a way-station between the hypothalamus and forebrain, receives projections from the mammillary bodies and hippocampal area, and projects to the anterior cingulate region (Area 24). Area 24, in turn, projects to the caudate nucleus and is an important frontal suppressor area (Fulton[11]).

Direct frontohypothalamic connections have been demonstrated by Ward and McCulloch[28] by strychninizing the orbital surface, and also by histologic methods (Le Gros Clark and Meyer,[4] von Bonin and Green,[26] Beck, Meyer and Le Beau[1]).

SELECTION OF PATIENTS

Each patient had been committed to the mental institution, and had received intensive psychiatric therapy, with unsatisfactory results, prior to referral to the Neurosurgical Unit for consideration of psychosurgery. The majority of these patients resided on closed wards, restricted to disturbed patients. The average period of institutionalization preceding surgery was 8 years. Psychiatric consultations (R.E.H.D. and W.B.McG.) were made independently, and surgical intervention was recommended only if the mental illness was associated with some degree of emotional responsiveness. The estimation of emotional "charge" was based upon the complaints, behavior, and autonomic status of the patient, and, to a degree, constituted the major criterion for operation. The indications and contraindications for lobotomy as used by our group are essentially the same as described by Freeman and Watts.[10]

Preoperative studies also included psychometric, electroencephalographic, pneumoencephalographic, spinal fluid, and medical evaluations in almost all cases prior to neurosurgical recommendations.

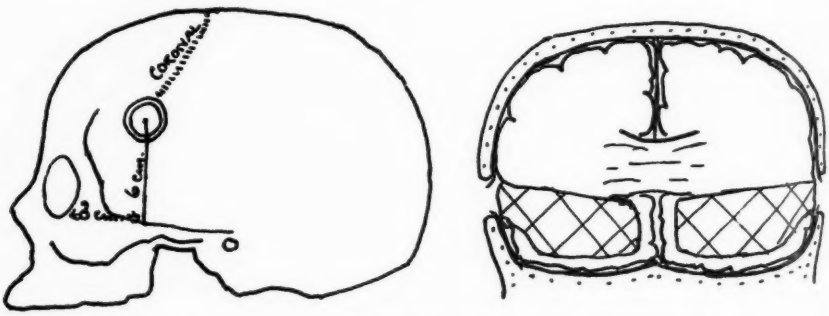
The group of patients who were selected for orbitofrontal lobotomy were of the following diagnostic categories:

Schizophrenia		43 patients
Catatonic	20	
Paranoid	17	
Hebephrenic	5	
Unclassified	1	
Manic-depressive		5 patients
Manic phase	5	
Involutional psychoses		2 patients
Paranoid type	2	
Psychoneuroses		1 patient
Anxiety, cachexia	1	
Miscellaneous disorders		4 patients
Paranoid conditions	2	
Mental deficiency agit. depr. psychosis	1	
Epilepsy with psychosis paranoid type	1	
		55 patients

SURGICAL TECHNIQUE

Intravenous sodium pentothal and endotracheal nitrous oxide and oxygen were administered by an anesthesiologist. Scalp measurements conformed to those described in the precision method standard lobotomy operations by Freeman and Watts[10] and were marked with gentian violet. The low frontal area of the scalp was infiltrated with 1 per cent procaine, preparatory to incision of the skin. The incision was placed behind the hairline, long enough to admit a 1½-inch crown trephine. The trephination was located at a point 6 cm. perpendicular to a marker placed 3 cm. posterior to the lateral rim of the orbit along the zygoma (Fig. 2). The dura was opened in a cruciate manner, retracted, and the cerebral cortex was then inspected

for pathology. A brain cannula was passed directly medially in the plane of the marker on the drape, corresponding to a previously measured point, 11 cm. posterior to the glabella, in the midline. The position of the anterior horn of the lateral ventricle was determined. A cortical incision followed and orbitofrontal lobotomy was accomplished by dissection with the sucker and cottonoid pads, under direct vision, following the plane of the midline marker, inferiorly to the cortex above the sphenoidal ridge, thus accomplishing a lower quadrant frontal lobotomy. Hemostasis was rarely difficult with the aid of silver clips, electrocoagulation and Gelfoam. A large cottonoid pack was left in place after doing one side, and the procedure was repeated on the opposite side before closure was made, first on the original side and finally on the secondary side (Fig. 3).



FIGS. 2 and 3. (*Left*) Landmarks for 1½-inch crown trephinations (Freeman-Watts measurements). (*Right*) Orbitofrontal lobotomy, coronal view.

RESULTS OF ORBITOFRONTAL LOBOTOMY

Fifty-five patients have now been studied by us for 6 to 54 months following orbitofrontal lobotomy. The clinical results and complications of this therapy are tabulated in Table 1.

Evaluation of results in each patient was based on a combination of psychiatric and psychometric determinations, the social adjustment of the patient, the judgment of relatives and of the patient about his mental status and information obtained from questionnaires submitted to relatives.

Twenty-nine patients (52.5 per cent) were improved to the point that they have been discharged from the hospital and are now living at home. Of these, 8 are independent and self-supporting, 11 are partially self-supporting, but require some supervision, and 10 require care and observation at home.

Twenty-five patients (45.45 per cent) have remained in the hospital, with the majority (17 patients) becoming improved to the degree that they could be transferred to open wards, ground crews, the farm, the laundry, the kitchen, etc., no longer requiring close supervision and treatment on closed or disturbed wards. Six patients have shown no improvement and 2 are worse (both suffered surgical complications). One patient expired 1 week

TABLE 1

Results of orbitofrontal lobotomy (55 patients) during 6–54 months

Diagnosis		At Home			In Hospital			Dead
		Indep.	Impr.	Dep.	Impr.	Unimpr.	Worse	
Schizophrenia	43							
Catatonic	20	2	5	5	6	2		
Paranoid	17	2	2	2	7	2	1	1
Hebephrenic	5	1		1	2	1		
Unclassified	1						1	
Totals		5	7	8	15	5	2	1
Manic-depressive psychosis	5							
Manic phase	5	1	2	1	1			
Involutional psychosis	2							
Paranoid type	2	1		1				
Psychoneurosis	1							
Anxiety neurosis, severe with cachexia	1	1						
Miscellaneous disorders	4							
Paranoid conditions	2		1			1		
Mental deficiency, with agit. dep. psychosis	1		1					
Epilepsy with psychosis paranoid type	1				1			
Totals		8	11	10	17	6	2	
		29			25			1
		46				6	2	

Complications:

Cerebral thrombosis, causing death (associated diabetes and hypertension)	1 patient
Meningoencephalitis, with partial recovery	2 patients
Brain abscess, bifrontal, recovery	1 patient
Epilepsy, due to procedure	3 patients
Postoperative hemorrhage	0
Urinary incontinence, more than 3 days	0

postoperatively because of cerebral thrombosis and bronchopneumonia. This patient was also diabetic and hypertensive; the complications occurred in spite of the added precautions of management of such bad risk problems.

It is apparent that 46 patients, or 83 per cent, were improved by orbitofrontal lobotomy in varying degrees, with 29 of these patients at home and 17 still in the hospital. The average duration of the mental illness in these cases was 8 years.

Three patients sustained infections due to the surgery; 1 made an excellent recovery, but the other 2 are now considered to be worse than prior to the operation. One of these complications resulted from the patient picking out his own sutures in an unguarded moment. Another followed obvious contamination of the operative field by dust blown out of the antiquated cooling system for the operating room. (This, at least, led to immediate installation of refrigeration cooling methods.) We have no explanation for the third instance of postoperative infection.

Two patients (Cases 4 and 39) suffered from convulsive seizures before surgery, and in 3 additional cases, to date, convulsions developed postoperatively (Cases 9, 15 and 43). The incidence of postsurgical epilepsy, therefore, is 6 per cent, in a 6- to 54-month follow-up following orbitofrontal lobotomy in 55 patients.

We have had no examples of postoperative hemorrhage, and are inclined to believe this may be the result of constant control of hemostasis by applying a time-honored principle of good surgical technique, namely, adequate exposure of the area of operation.

There have been no instances of persistence of urinary incontinence beyond the first 2 or 3 days.

ELECTROENCEPHALOGRAPHIC OBSERVATIONS

EEG studies on patients who are treated with psychosurgery are said to be of value, preoperatively, postoperatively, and with particular reference to postsurgical epilepsy.

There has been considerable uniformity among the few reports of EEG observations on patients subjected to frontal lobotomy and its modifications (Davis,[7] Cohn,[5] Stevens and Mosovich,[25] Murphy,[17] and Zigarelli[29]). High-potential, slow-wave activity in both frontal leads, and increased sensitivity to hyperventilation are usually present during the early postoperative period, with the standard lobotomy operation. Enhancement of the regularity and frequency of the occipital alpha pattern, in comparison to preoperative records, has occasionally been mentioned.

Lesions, as identical as possible, were placed in the orbitofrontal areas bilaterally, following the technique as described in our 55 patients. EEG studies were made, utilizing 8-channel Grass equipment, with monopolar recordings during the waking, hyperventilated, drowsy and sleeping states.

EEG studies were obtained on 25 patients prior to surgery, and on 34 patients postoperatively. The postsurgical studies were made at graded intervals of 2 weeks, 12 months and 2 years postoperatively. Twelve of these 34 patients showed temporary or permanent EEG abnormalities (Cases 11, 17, 18, 20, 24, 29, 32, 38, 39, 41, 42, 49). There were:

Temporary bifrontal high-potential slow-wave changes—5 cases (17, 18, 20, 29, 39, 42)
Permanent bifrontal high-potential slow-wave changes—3 cases (41, 42, 49)
Permanent right frontotemporal slow-wave focus—1 case (11)

Diffuse bifrontal-temporal diphasic spiking—1 case (38)
Low-amplitude asymmetry, left hemisphere—1 case (32)
Right anterior temporal slow-wave and negative spike focus—1 case (24).

Convulsive disorders that complicate frontal lobotomy have been reported to be variable in onset, but they usually occur within the first year, and thus these patients show clinical and EEG abnormalities similar to those of patients who have sustained acute head injuries. Three patients in whom seizures developed following orbitofrontal lobotomy (Cases 9, 15, 43) had essentially normal EEG studies.

In our experience, the EEG studies have been of considerable academic interest, but of little practical value in this series of cases.

PNEUMOENCEPHALOGRAPHIC OBSERVATIONS

In the majority of our patients selected for psychosurgery pneumoencephalographic studies have been made, particularly if there was any clinical suggestion of associated neuropathology. In this series of 55 patients, air studies were made in 36 instances prior to operation. The findings may be summarized as follows:

Normal pneumoencephalograms		25 cases
(Poor ventricular filling in 4 of these cases, but excellent visualization of the subarachnoid spaces)		
Abnormal pneumoencephalograms		11 cases
Diffuse cortical atrophy	3	
(Cases 14, 35, 53)		
Localized cerebral atrophy	8	
Both frontal areas (Cases 25, 32, 43, 48)		
Left frontal area (Cases 17, 51)		
Right frontal area (Case 55)		
Right temporal lobe (Case 16)		

We were unable to correlate the presence of cerebral atrophy, diffuse or localized, with the clinical features of the mental illness, the electroencephalographic findings or the response to orbitofrontal lobotomy. Four of the better clinical results occurred in patients with pneumoencephalographic evidence of cortical atrophy.

PSYCHIATRIC EFFECTS OF ORBITOFRONTAL LOBOTOMY

The so-called "orbital syndrome" of increased motor activity, extroversion, and euphoria, which has been described in man (Reitman[20]) and macaque (Ruch and Shenkin[21]) following ablation of the orbital surfaces of the frontal lobes, has not been confirmed by our series of operations in this area.

Orbitofrontal lobotomy was observed to create a release from anxiety, increased friendliness and sociability, and acceptance of fixed circumstances that had previously caused a sense of frustration. These features, however,

did not occur to the degree that frequently occurs after "standard" frontal lobotomy. There was little evidence of changes of personality in respect to loss of social consciousness, ambition, imagination and foresight that have been associated with more radical procedures.

SUMMARY AND CONCLUSIONS

Orbitofrontal lobotomy was performed on 55 patients, each of whom had been committed to a state mental institute for an average of 8 years.

Twenty-nine were discharged from the hospital. Eight are entirely independent, 11 partially self-supporting, and 10 remain under supervision at home.

Twenty-five patients have remained in the hospital, with 17 showing improvement enough for transfer to open wards and part-time work. One patient expired but was not considered to be an operative fatality.

Convulsive seizures following lobotomy have occurred in 3 patients. There have been no instances of postoperative hemorrhage or of persistent urinary incontinence.

Relatively little correlation of clinical symptoms with electroencephalographic and pneumoencephalographic studies was observed.

Orbitofrontal lobotomy was relatively effective in this series of patients in normalizing emotional responsiveness, without the production of the undesirable blunting of personality, or the usual incidence of postoperative complications that accompanies less selective procedures of this nature.

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THE ELECTROENCEPHALOGRAM IN SUBDURAL HEMATOMA

LEWIS L. LEVY, M.D., LUDWIG H. SEGERBERG, M.D., RICHARD P. SCHMIDT, M.D., RICHARD C. TURRELL, M.D., AND EPHRAIM ROSEMAN, M.D.

Sections of Neurology, Neurosurgery and Electroencephalography, University of Louisville School of Medicine, and the Louisville General Hospital, Louisville, Kentucky

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THE most adequate method of diagnosing subdural collection of blood is by complete surgical exploration. Although much aid has been obtained from the electroencephalogram (EEG) in the study of head injuries, the literature tends to be confusing in the interpretation of its value in indicating the presence of subdural hematoma.[1–3,5–14]

The reader is referred to the excellent reviews of Smith, Mosberg, Pfeil and Oster[13] and of Marsh, Hjartarson and Courville[9] for a comprehensive discussion of the literature on the subject. The generally accepted EEG findings in unilateral subdural hematoma are ipsilateral reduction in amplitude of the alpha activity and/or a delta focus.

PRESENT STUDY

In the present study the electroencephalographic findings in 60 cases of severe head injuries were reviewed. Attempts were made to establish the diagnosis of subdural hematoma on the basis of the initial records. Serial records were examined for additional diagnostic clues.

In all 60 cases the question arose some time during the hospital course of: (1) the possibility of the presence of a subdural hematoma and (2) the need for exploratory surgery. This problem of the necessity for operation was a particularly pressing one in the cases of acute head injuries. In all instances there was an initial period of coma following the injury, bloody cerebrospinal fluid (CSF), a subsequent period of mental depression and/or increasing abnormal focal neurologic signs. Any of these 60 patients by such clinical criteria could have been suspected of having either unilateral or bilateral subdural hematomas.

For the most part a Grass 8-channel ink-writing oscillograph was used. A minimum of 13 needle (27 gauge) electrodes were inserted into the scalp and ear lobes, using the standard ground and bipolar runs (with reference to each other, to the ears and the vertex).

RESULTS

Thirty of the 60 patients had unilateral subdural hematomas (Table I). The remaining 30 had neither subdural nor epidural hematomas. All patients having bilateral hematomas and children under 10 years of age are

TABLE 1

Total number of cases of subdural hematoma		30
1. Cases proven at operation	26	
2. Cases found at autopsy	4	
Total number of cases of head injury without subdural hematoma		30
1. Bilateral burr hole exploration negative	16	
2. No subdural or intracerebral hematoma at autopsy	3	
3. Negative X-ray pneumograms	5	
4. Clinical improvement after 3 or more months	6	

Table 1 demonstrates that there were 30 proven cases of unilateral subdural hematoma either at operation or autopsy. In the additional 30 cases of head injury without subdural hematoma, the clinical picture was the same, namely, initial period of coma, hemiparesis, and bloody cerebrospinal fluid.

excluded from this study, since the EEG patterns in these groups are heterogeneous and need further study.

Table 2 divides these cases, for purposes of convenience only, into the acute (0–5 days), subacute (6–15 days) and chronic head injuries (16 days

TABLE 2

Interval of time between injury and first EEG

	0–5 Days		6–15 Days		16+ Days		Total	
Subdural	19		4		7		30	
Head injury	20		6		4		30	
Total	39		10		11		60	
	Subd.	H.I.	Subd.	H.I.	Subd.	H.I.	Subd.	H.I.
Ipsi. Dec. Amp. SWF	11	11	3	4	4	2	18	17
Ipsi. Dec. Amp. Alone	4	2	1	1	0	0	5	3
Ipsi. SWF Alone	0	1	0	0	0	1	0	2
Ipsi. SWF Contra Dec. Amp.	1	0	0	0	2	0	3	0
Ipsi. Dec. Amp. Contra SWF	0	2	0	0	0	0	0	2
Contra SWF Contra Amp.	1	0	0	0	0	0	1	0
No Focal Abnormality	2	4	0	1	1	1	3	6
Totals	19	20	4	6	7	4	30	30

The head injuries (H.I.) and subdural hematomas (Subd.) are divided arbitrarily into acute (0–5 days), subacute (6–15 days) and chronic (16 days). This period indicates the time in days that the EEG was taken following the head injury. It can be seen that the EEG abnormalities in the two groups, taking into account the factor of time, have an almost identical distribution.

Ipsi. = ipsilateral. Dec. = decrease. Amp. = amplitude. SWF = slow-wave focus. Contra = contralateral.

TABLE 3

Clinical signs of subdural hematoma

Contralateral signs	22 cases
Ipsilateral signs	5 cases
No focal signs	3 cases

In the 5 cases of subdural hematoma with ipsilateral hemiparesis there was homolateral amplitude reduction and/or slow-wave focus in the initial EEG.

and over). All possible EEG patterns involving the two parameters of presence or absence of delta activity and amplitude asymmetry are listed. It will be noted that although an ipsilateral decrease in amplitude and/or slow-wave focus was present in 43 of the 60 cases, the distribution in those with and without subdural hematomas was about equal. Further perusal of Table 2 shows that all possible EEG combinations occur in relatively equal numbers in both types of cases.

Table 3 indicates that 5 of the 30 patients with subdural hematoma had a hemiparesis on the side of the hematoma. This group of 5 had an ipsilateral decrease in amplitude and/or slow-wave focus.

As noted in Table 4, seven members of the Neurology Department, whose electroencephalographic experience varied from 1 to 14 years, were shown the initial EEGs of all 60 cases with the names and histories deleted. Those tested were asked to indicate: (1) which records indicated the presence of subdural hematoma, (2) the side of the hematoma, (3) which were not subdural hematomas and (4) those EEGs that they thought were inconclusive. No one person correctly picked more than 2 out of 3 of the hematomas.

TABLE 4

Examiner	Experience (years)	Subd. Correctly Picked	H. I. Correctly Picked	H. I. Called Subd.	Subd. Called H. I.	No Decision	Total	% Subd. Called Correctly	% H. I. Called Correctly
E. R.	13	12	17	12	16	3	60	50	51
L. S.	1	11	14	16	16	3	60	40	47
T. D.	7	10	25	5	16	4	60	67	61
W. S.	1	14	17	10	14	5	60	60	55
R. T.	2	9	16	12	15	8	60	43	51
S. A.	14	16	20	9	12	3	60	64	63
L. L.	2	5	23	7	20	5	60	42	54
Total	40	77	132	71	109	31	420		
Av.	5.7	11	19	10	15.5	4.5	60	52	55

Nine members of the Neurology Department with EEG experience varying from 1 to 14 years took the test. In this test they were shown the initial EEGs of all 60 patients, with deletion of case histories. They were asked to select: (1) those records that they thought indicated a subdural hematoma, (2) the side of the hematoma, (3) those records that did not indicate a hematoma, and (4) those EEGs that were inconclusive.

It is to be noted that the percentage of error was high. The range of those who correctly picked the subdural hematomas was from 40 to 67 per cent, with an average of 52 per cent.

Subd. = subdural. H.I. = head injury.

E.R., with the most concentrated clinical and EEG experience in this field, made a 50 per cent error. The entire group correctly picked 52 per cent of the subdurals and 55 per cent of the nonsubdurals on the basis of the initial EEG findings.

The percentage of correct EEG diagnoses was not altered appreciably by taking into account the various types of recordings, e.g., scalp to ear, scalp to vertex, ground and triangulation. Serial records in both groups followed similar patterns.

DISCUSSION

Review of the literature would give the impression, for the most part, that given an individual who has had a head injury, a presumptive diagnosis of subdural hematoma can be made on the basis of the electroencephalographic changes. The electrical abnormalities most commonly cited are ipsilateral decrease in amplitude with or without associated slow-wave focus.

In the series of 60 cases of severe head injury reported here an initial period of coma and bloody CSF followed by a period of clinical worsening, usually with the appearance of focal neurologic abnormalities, were common to all. The EEG abnormalities were the same in all regardless of whether a subdural hematoma was present or not. The number of proven subdural hematomas was 30 of the total 60 cases.

In 5 cases of proven subdural hematoma with homolateral focal signs, e.g., hemiparesis, there was an associated ipsilateral reduction in amplitude and slow-wave focus. This combination was not seen in any of the remaining 55 cases. (In a subsequent case which did demonstrate these findings, however, operation failed to reveal a subdural hematoma.) Thus, with the possible exception of this small group it is felt that the initial EEG is of no aid in differentiating the operative from the nonoperative cases.

The presence of blood in the subdural or the epidural spaces probably plays no factor in the reduction of amplitude on the side of the lesion. This is seen to persist following operative removal of the clot and in subcortical lesions of a nontraumatic nature.

Figs. 1–5 demonstrate some illustrative cases and some of the pitfalls that may be encountered in the EEG study of head injuries with particular reference to the recognition of subdural hematomas. Fig. 1 A shows an EEG taken 15 days after injury. Although it is a relatively normal one, with the exception of slight amplitude reduction on the right side, the patient became worse clinically. Subsequently, negative bilateral exploration was made and the patient returned to normal health. The EEG shown in Fig. 1 B, taken 1 day after head injury, looks very similar, but this patient's clinical course and EEG worsened. Four days after trauma a large subdural hematoma was evacuated from the left side, Thus, in both cases, there were only mildly abnormal initial EEGs; in both there was subsequent increase in clinical symptoms.

Fig. 2 shows 2 more cases of head injury, one with (Fig. 2 A) and the

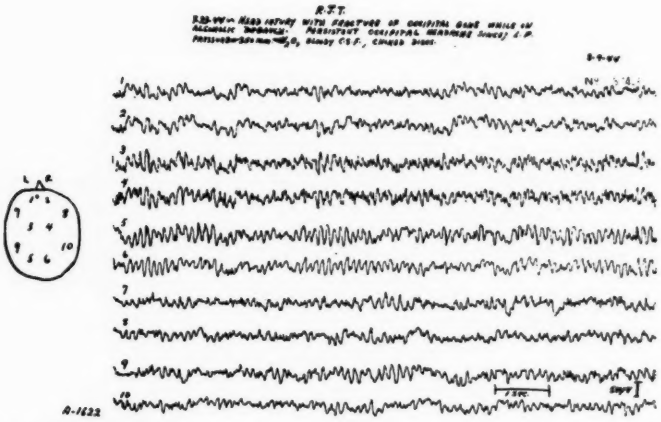

FIG. 1 A. *R. J. T.* Head injury with initial coma on July 23, 1944. Persistent left hemiparesis, choked discs and elevated CSF pressure. Because of suspicion of subdural hematoma, bilateral trephination was made on Aug. 10, 1944, and showed only contused cortex on the right. Subsequent complete clinical improvement.

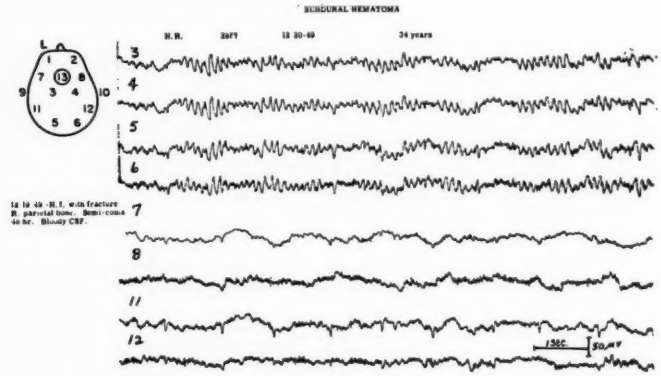

FIG. 1 B. *H. R.* Head injury with initial coma 24 hours prior to EEG. Because of worsening of clinical picture, bilateral burr-hole exploration was made 4 days after injury and a large subdural hematoma was evacuated from the left side.

Note that the initial EEGs of these 2 patients are similar. The only abnormalities are a slight decrease in amplitude and delta focus (on the right side in Fig. 1 A and on the left side in Fig. 1 B).

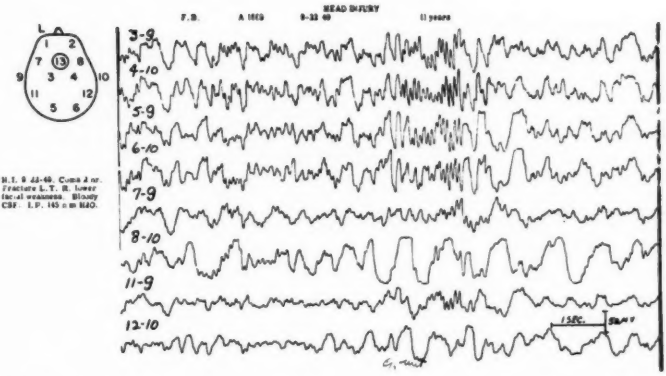

Fig. 2 A. *F. B.* Sept. 22, 1949, severe head injury with initial period of coma lasting 2 hours. Negative bilateral burr-hole exploration Sept. 22, 1949. Subsequent complete clinical improvement

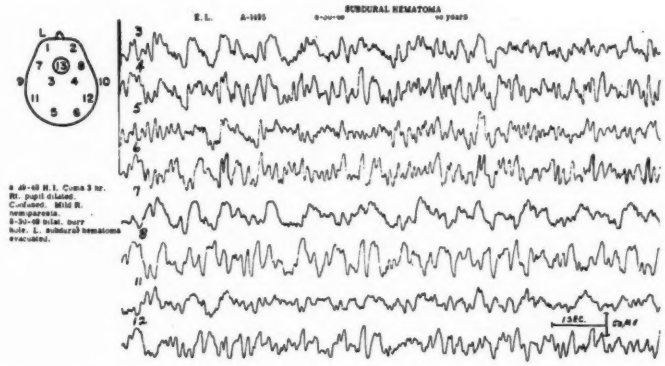

Fig. 2 B. *E. L.* Head injury with 3-hour period of coma 24 hours prior to EEG. Bilateral exploration showed large left subdural hematoma.

Note that although the clinical histories and EEGs are similar, only one (E.L.) had a subdural hematoma. The common EEG finding in both cases, however, was a decrease in amplitude, seen best in the left temporal region.

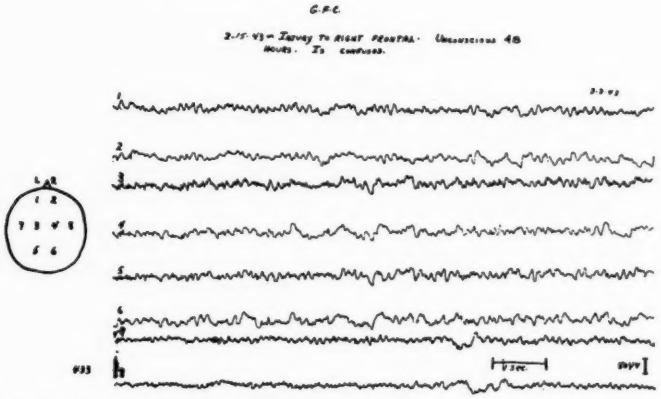

FIG. 3 A. *G. F. C.* Severe head injury, 16 days prior to EEG, with left hemiparesis and confusion. Because of persistent abnormal clinical signs, bilateral burr-hole exploration was made Mar. 5, 1942 and was negative. Subsequent return to clinical normalcy.

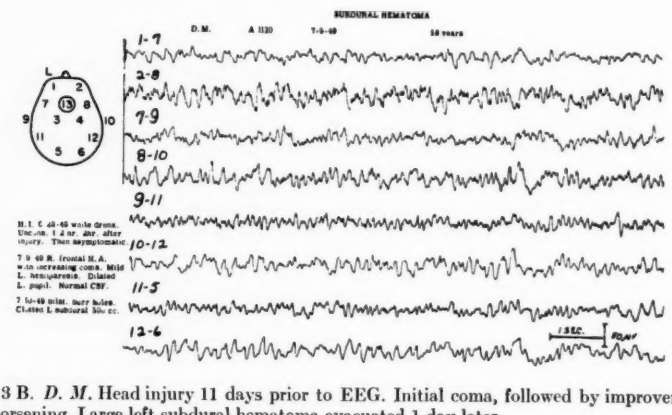

FIG. 3 B. *D. M.* Head injury 11 days prior to EEG. Initial coma, followed by improvement, then clinical worsening. Large left subdural hematoma evacuated 1 day later.

Note that the common EEG finding in both cases is a reduction in amplitude (on the right side in Fig. 3 A and on the left side in Fig. 3 B).

other without (Fig. 2 B) subdural hematoma. In both instances the EEGs taken within 24 hours after the injury demonstrate very abnormal and yet very similar initial records. They are moderately slow and show an ipsilateral amplitude reduction and homolateral slow-wave focus. Again, the difficulty in differentiation of the two on basis of the EEG findings would seem impossible.

Fig. 3 shows a similar difficulty in the recognition and differentiation of

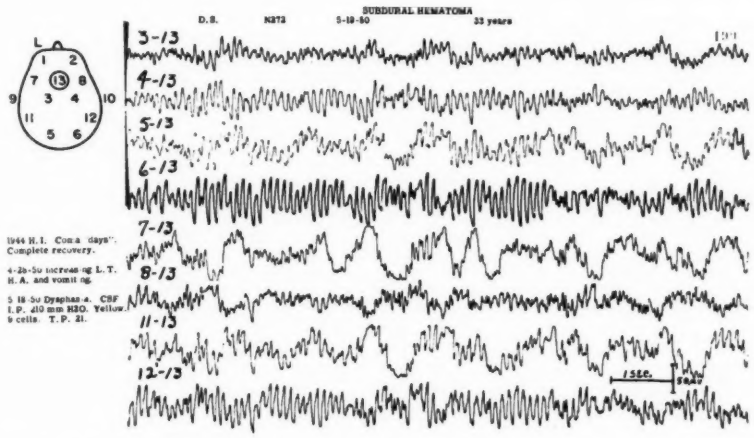

FIG. 4. *D. S.* Head injury 6 years prior to EEG. Asymptomatic in interim, but progressive development of headache, dysphasia and coma 1 day prior to EEG. Subsequent removal of large chronic subdural hematoma and membrane on left side.

Note reduction in the amplitude and marked circumscribed delta focus in left temporal region.

2 traumatic cases of a subacute or chronic nature. Fig. 3 A demonstrates an EEG taken 16 days after injury, followed by negative bilateral exploration and return to normalcy. In the case represented in Fig. 3 B a left subdural hematoma had been removed 11 days after injury and 1 day after the EEG. Both EEGs look similar in that they are mildly dysrhythmic, show mild amplitude reduction and a delta focus. In Fig. 3 A these abnormalities are seen on the right side and in Fig. 3 B they are on the left side.

Fig. 4 illustrates the EEG picture in a case of chronic subdural hematoma which was asymptomatic for 6 years and then dysphasia and coma rapidly developed. At operation subsequently a large thick membrane covering almost the entire left hemisphere was removed. The right side was normal. The EEG picture presented is not unlike that seen in many types of gross hemispheric lesions.

Fig. 5 demonstrates the EEG picture seen in 5 cases of subdural hematoma with ipsilateral hemiparesis. The patient illustrated had been injured 19 days prior to the first EEG (Fig. 5 A). In spite of the left hemiplegia, but

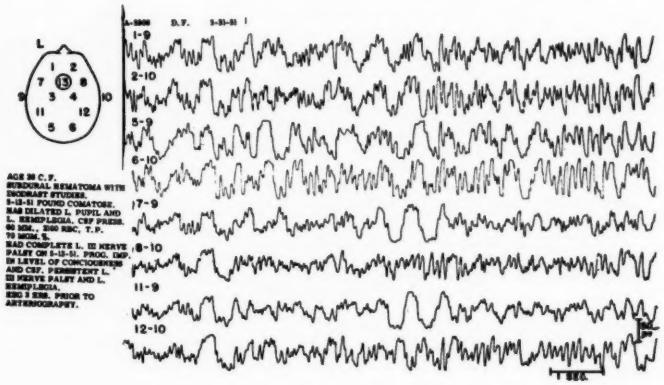
AGE 38 C. F.
SUBDURAL HEMATOMA WITH DIODRAST STUDIES.
5-12-51 FOUND COMATOSE.
R&B DILATED L. PUPIL AND L. HEMIPLEGIA. CSF PRESS. 60 MM., 2565 REC. T. P. 70 MGM. %.
R&D COMPLETE L. III NERVE PALSY ON 5-13-51. PROG. DEP. IN LEVEL OF CONSCIOUSNESS AND CSF. PERMITEXT L. III NERVE PALSY AND L. HEMIPLEGIA.
EEG 1 HR. PRIOR TO ARTERIOGRAPHY.
D.F. 5-21-51
1-9
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FIG. 5 A

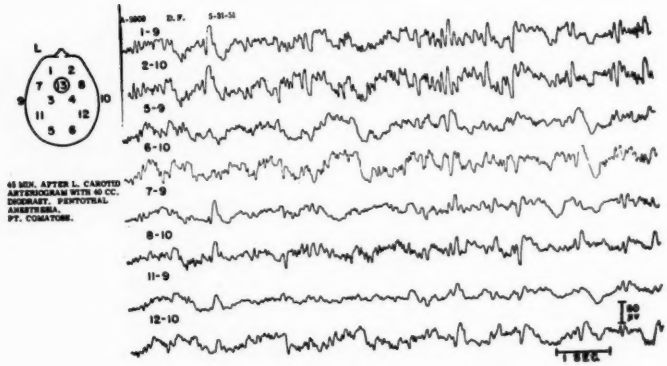

FIG. 5 B

because of the reduction of amplitude and slow-wave focus on the left side, a left carotid arteriogram was done and showed a picture compatible with that seen in subdural hematoma. Subsequent operation revealed a large hematoma on the left side; the right side was normal. Fig. 5 B shows initial depression of the EEG 45 minutes following the injection of a total of 40 cc. of 35 per cent diodrast. Subsequent EEGs taken 4 (Fig. 5 C) and 24 hours (Fig. 5 D) after arteriography demonstrate a worsening of the EEG picture associated with increased clinical symptoms.[4] This occurred in spite of the fact that for the first 19 days the patient was under observation, there had been progressive clinical and EEG improvement.

CONCLUSIONS

The electroencephalographic analysis of 60 cases of head injury is presented with the view in mind of differentiation of those patients who have

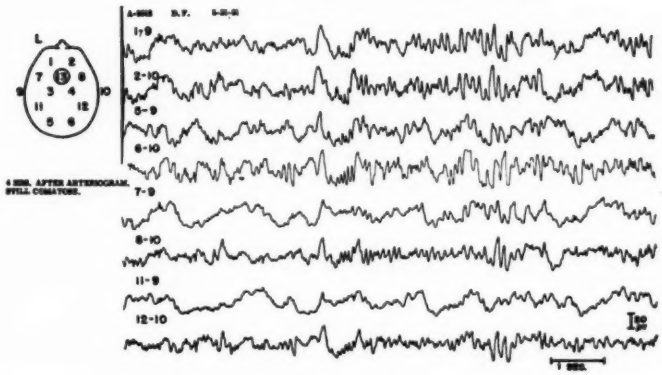

FIG. 5 C

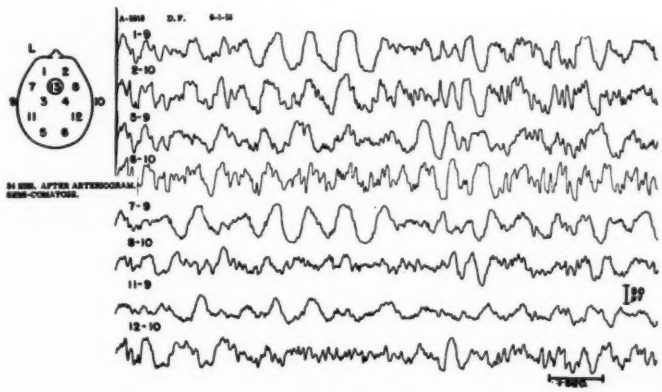

FIG. 5 D

FIG. 5. *D. F.* Found comatose on May 12, 1951. Left 3rd nerve paralysis, left hemiplegia and bloody CSF. Initial clinical improvement. EEG taken 19 days later (Fig. 5 A) showed reduction in amplitude and delta focus in left temporal region. Because of this, and in spite of the left hemiplegia, a left carotid arteriogram was done and demonstrated a picture compatible with a subdural hematoma on this side. The patient remained comatose subsequent to arteriography and a subdural hematoma was evacuated on the left side.

Note the persistent amplitude reduction and delta focus on the side of the hematoma (Fig. 5 A, B, C and D). In Fig. 5 B, taken 45 minutes after left carotid arteriography, there is a generalized suppression. Subsequently, there is marked slowing of the EEG (Fig. 5 C and D), concomitant with aggravation of the clinical findings.

subdural hematoma from those who do not. Thirty had proven subdural hematomas and of the other 30, 16 had negative bilateral explorations, 3 showed no evidence of hematoma at autopsy, and 11, of which 5 had normal pneumograms, returned to clinical normalcy. No data are presented on bilateral subdural hematomas or the EEG picture in infants.

The findings indicate that the initial EEG is identical in these 2 groups of head injuries with and without subdural hematoma and hence make their differentiation impossible. The parameters of ipsilateral reduction in amplitude and slow-wave focus are similarly present in both regardless of whether the initial EEG is taken in the acute, subacute or chronic stage. Hence, with one possible exception, noted below, it would seem that the initial EEG is of no value in the differentiation of the "operative" from the "nonoperative" types of head injuries, particularly insofar as unilateral subdural hematomas in adults are concerned.

Five cases of subdural hematoma with ipsilateral paralysis are presented. In all of these instances the hematoma was present on the side of the amplitude reduction with the slow-wave focus.

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AUTONOMIC PATHWAYS IN THE SPINAL CORD

DONALD A. JOHNSON, M.D.,* GRACE M. ROTH, PH.D.,† AND WINCHELL McK. CRAIG, M.D.‡

Mayo Foundation, University of Minnesota, and Sections of Physiology and Neurologic Surgery, Mayo Clinic, Rochester, Minnesota

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Most of our knowledge about the autonomic pathways within the spinal cord in man stems from the findings of Foerster on patients following anterolateral chordotomy for intractable pain. Foerster, as well as Guttmann,[6] found anhidrosis after anterolateral chordotomy and also concluded that the pathways for sweating ran in the anterolateral column of the spinal cord. Foerster and Gagel[5] believed that the pathways for sweating in the spinal cord travel in the most dorsal part of the anterolateral columns, adjacent to the pyramidal tracts, because the 2 patients in whom they were able to demonstrate anhidrosis also had Babinski reflexes postoperatively. Because the anhidrosis was not permanent, they concluded that the pathways for sweating also ran in other quadrants of the spinal cord.

Later, in 1936, Foerster[4] demonstrated changes in vasoconstrictor reflexes after bilateral chordotomy. He expressed the belief that the efferent arm of these reflexes also was situated in the anterolateral column of the spinal cord. Because he observed changes in vasoconstrictor reflexes, not after unilateral, but only after bilateral chordotomy, he concluded that vasoconstrictor pathways to both sides of the body are represented in each anterolateral quadrant of the cord. Therefore, he thought that the vasoconstrictor pathways were interrupted only when the chordotomy was bilateral and adjacent to the pyramidal tracts. During this same period, Babtchine[1] reported elevation of the cutaneous temperatures after unilateral chordotomy. He believed that the vasomotor and pyramidal tracts run closely together, because in each case there was also a Babinski reflex on the side of the chordotomy.

In Foerster's opinion the somatotopic arrangement of the fibers in the spinal cord was the same for those fibers mediating impulses to the sweat glands as it was for those mediating impulses to the blood vessels. He concluded that the pathway to the arm was located medially in the cord and the pathway to the leg was located laterally. This concept of spinal cord anatomy is illustrated in Fig. 1.

Shortly afterward, in 1939, List and Peet[10] could neither confirm nor deny Foerster's conception of the somatotopic arrangement of the auto-

* Fellow in Neurosurgery, Mayo Foundation, University of Minnesota.
† Section of Physiology, Mayo Clinic, Rochester, Minnesota.
‡ Section of Neurologic Surgery, Mayo Clinic, Rochester, Minnesota.

nomic fibers in the spinal cord. They suggested that vasoconstrictor and sudomotor impulses might pursue different and distinct paths in the cord since in 1 case they found hyperthermia in the ipsilateral arm following chordotomy, without changes in the sweating function.

Falconer and Lindsay[3] reported data on 2 cases in which chordotomy resulted in diminution of sweating, most marked above the level of the chordotomy. Hyndman and Wolkin[7] also had 1 case in which sweating was abolished above the level of a bilateral chordotomy. In these cases the pyramidal tracts were simultaneously impaired, and the authors agreed that the autonomic fibers reside very close to or within the pyramidal tracts.

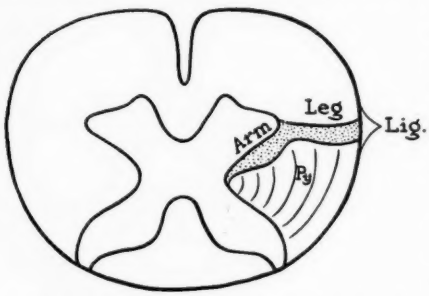

FIG. 1. Autonomic pathways in the spinal cord. (Redrawn after Foerster[4].)

Because of the lack of agreement of previous investigators and the opportunity to study a group of patients after anterolateral chordotomy for intractable pain, the question arose as to whether further information could be gained by carrying out such physiologic tests as reflex sweating on exposure to a baker and skin temperature measurements after anterolateral chordotomy. Thus the present investigation was begun.

PROCEDURE

Patients. Anterolateral chordotomy was carried out on 5 patients because of intractable pain. Neurologic examination was performed before and after anterolateral chordotomy in each patient.

Operation. After removal of the spines and laminae of the 7th cervical and 1st and 2nd thoracic vertebrae the dura was opened and the dentate ligaments were divided. Anterolateral chordotomy was performed between the 1st and 2nd thoracic levels by rotating the spinal cord and dividing the anterolateral tracts at depths from 5 to 7 mm.

Physiologic Tests. Skin Temperatures. Basal metabolic rates and skin temperature measurements of the fingers and toes were determined[15] after anterolateral chordotomy. Control studies before operation were attempted but, because of the severe pain, basal observations could not be determined.

Before the tests the subjects were fasted for 15 hours, and during the test they wore light-weight short pajamas and lay supine on comfortable beds. Data were obtained in a room in which the constant temperature was 25.5°C. (78°F.) and the relative humidity was 40 per cent. The temperatures of the plantar surface of the first and third toes of both feet and the volar side of the distal phalanges of the first and third fingers were determined by means of copper-constantan thermocouples. The observations were made at

intervals of 10 minutes for 1 to 2 hours. In the normal person there is a gradient of skin temperature from the head to the feet, with the lowest skin temperatures in the toes.

Sweating Test. The cobalt chloride method[14] of determining the region of anhidrosis was used after anterolateral chordotomy. Cobalt chloride in a saturated alcoholic solution is deep blue but turns to bright pink on addition of water. The alcoholic solution is striped over the area to be examined. An aluminum heating cabinet large enough to cover the entire body except the head, containing a series of incandescent light bulbs which maintain a temperature of about 140°F., is placed over the patient. After 10 minutes or whenever sweating occurs the stripes become a bright pink. The change in color of the stripes indicates the varying degrees of sweating with considerable accuracy. No change in color indicates anhidrosis.

TABLE 1

Postoperative skin temperatures

Case	Anterolateral Chordotomy		Area of Anhidrosis	Skin Temperature degrees C.				Temperature Gradient of Fingers and Toes
	Side	Depth of Surgical Division mm.		Toes		Fingers		
				Right	Left	Right	Left	
1	Left	6	Bilateral above 5th thoracic	33.9	33.3	35.2	36	Normal
2	Left	5	None	31.2	33.0	27.0	28.9	Reversed
3	Left	7	None	28.1	32.5	25.7	25.3	Reversed
4	Right	6	Right arm	30.9	25.9	33.6	31.1	Normal
5	Left Right	6.5 5	Bilateral below 10th thoracic	30.9	26.0	33.6	31.1	Normal

RESULTS

Case 1.—A white woman, aged 60 years, had undergone abdominoperineal resection for carcinoma of the rectum 18 months before she was first seen at the Mayo Clinic. Six months after this operation pain had developed in the area of the coccyx. The pain had become progressively more severe and had extended down the right leg.

The results of neurologic examination were essentially negative. Since the pain was intractable and probably represented a metastatic process, left anterolateral chordotomy was performed. An incision 6 mm. deep was made into the left anterolateral quadrant of the cord at the level of the 1st thoracic vertebra. Postoperatively there was a sensory level for pain and temperature on the right corresponding to the lower border of the 4th thoracic dermatome. There was neither a Babinski reflex nor hyperreflexia following chordotomy. There was complete relief of pain on the

right. A postoperative sweating test showed almost complete anhidrosis above the 5th thoracic level (Fig. 2). Postoperative cutaneous temperature measurements are shown in Table 1.

In the few reported cases in which anhidrosis has been present following chordotomy, it usually has been present ipsilaterally below the level of the chordotomy. This also has been our experience. Case 1 was doubly unusual both in that the anhidrosis was above the level of the chordotomy and also in that it was bilateral after unilateral chordotomy. If the arrangement of the autonomic fibers in the spinal cord was as depicted in Fig. 1, section of the pathways to the arm without section of those destined to the leg would be virtually impossible, especially without considerable damage to the pyramidal tract. Indeed it has been held that this anatomic location of the autonomic pathways to the arm is the reason that they are not usually affected in chordotomy. However, in view of this case and others mentioned in this report, this explanation is probably not correct. The reason why the anhidrosis was bilateral is not clear. The skin temperatures (Table 1) suggest that vasomotor fibers were not affected; that is, vasomotor and sudomotor functions were dissociated.

FIG. 2. *Case 1.* Result of postoperative sweating test.

List and Peet[10] in their studies had 1 case (No. 17) in which unilateral chordotomy resulted in loss of sweating over the face on the ipsilateral side. There was no loss of sweating in the arms, but there was an ipsilateral cutaneous hyperthermia which did not involve the leg. It was this case that led them to suggest that vasomotor and sudomotor fibers might pursue distinct and separable pathways in the spinal cord.

In 2 cases of the series of cases reported by Hyndman and Wolkin,[7] sweating was abolished above the level of a chordotomy. Falconer and Lindsay[3] had 2 similar cases in their series. These cases demonstrate that the autonomic pathways within the spinal cord to the arm are actually more accessible to an approach from the lateral aspect of the cord than has been previously thought. As far as could be determined clinically, the pyramidal tract was not injured in any of these cases or in our cases. Thus it is unlikely that the anatomic relationship between the autonomic pathways and the pyramidal tracts is intimate.

Case 2.—The patient was a white woman, aged 53 years, who had intractable pain in the right leg caused by a recurrent myxosarcoma.

Left anterolateral chordotomy was performed at the level of the 2nd thoracic vertebra. An incision 5 mm. deep was made into the anterolateral quadrant of the cord. Postoperatively there was a loss of pain and temperature sensation on the right below the level of the 4th thoracic dermatome. No hyperreflexia or Babinski reflex was noted. A postoperative sweating test showed normal sweating over the entire body. Postoperative cutaneous temperatures are shown in Table 1.

The higher skin temperatures on the side ipsilateral to the chordotomy, as would be expected, and the reversal of the normal temperature gradient from fingers to toes suggest that vasomotor pathways were affected while sudomotor function remained intact.

Case 3.—A man, aged 67 years, suffered from postherpetic neuralgia over the distribution of the 5th and 6th thoracic dermatomes on the right. Conservative treatment did not afford relief. Left anterolateral chordotomy was done at the level of the 1st thoracic vertebra. An incision 7 mm. deep was made. Postoperatively there was no Babinski reflex on the left. The pain was relieved. There was loss of pain and temperature sense below T5 on the right.

The results of a postoperative sweating test were normal. Cutaneous temperatures after operation are shown in Table 1.

This case is similar to Case 2. The ipsilateral elevation of skin temperatures in the lower extremities is more marked than in Case 2. The dissociation of autonomic function is similar in the 2 cases.

Case 4.—The patient was a man, aged 71 years, who had intractable pain in the left side of the chest and abdomen and left leg caused by multiple myeloma. Neurologic examination gave no objective evidence of involvement of the spinal cord by the process. However, the cerebrospinal fluid contained 350 mg. of protein per 100 cc.

Right anterolateral chordotomy was performed at the level of the 1st thoracic vertebra. An incision 6 mm. deep was made. Postoperatively there was loss of pain and temperature sense on the left below the 8th thoracic dermatome. There were ptosis of the right eyelid and miosis of the right pupil, which persisted for 3 weeks. A postoperative sweating test (Fig. 3) showed loss of sweating in the right arm, except in the distribution of the T1 and T2 dermatomes. Sweating in the face was normal, though as mentioned, ptosis and miosis were present on the right.

Skin temperatures (Table 1) revealed a marked elevation of temperature on the right, involving the lower half of the body as well as the arm, in spite of the normal sweating over the lower portion of the body.

The dissociation of vasomotor and sudomotor function is quite distinct in this case.

An ipsilateral Horner's syndrome following chordotomy was reported by Falconer and Lindsay[3] and by Hyndman and Wolkin.[7] In these cases, the Horner's syndrome was associated with diminished thermoregulatory sweating over the face. Case 4 showed normal sweating over the face in the presence of ptosis and miosis.

FIG. 3. *Case 4.* Result of postoperative sweating test.

FIG. 4. *Case 5.* Result of postoperative sweating test.

Case 5.—The patient was a white woman, aged 62 years, who had low back and bilateral leg pain caused by a pelvic malignant lesion with metastasis. The results of neurologic examination were essentially negative. Bilateral chordotomy was done at the level of the 2nd and 3rd thoracic vertebrae. An incision 6.5 mm. deep was made on the left, and an incision 5 mm. deep of the anterolateral quadrant of the cord was made on the right. Postoperatively there was a loss of pain and temperature sense below T3 bilaterally.

A postoperative sweating test revealed anhidrosis below the level of the 10th thoracic dermatome (Fig. 4). Skin temperatures after operation are shown in Table 1.

COMMENT

Although this is a small series, these 5 cases demonstrate a dissociation of vasomotor and sweating functions caused by differential interruption of these pathways within the spinal cord. Further it seems evident that the restricted mediolateral somatotopic arrangement as depicted in Foerster's diagram (Fig. 1) must be considerably expanded within the anterolateral column of the cord and that a great part of the autonomic fibers in this column are not intimately related to the pyramidal tract.

The fact that vasomotor and sudomotor functions can be affected in a dissociated manner in the spinal cord is consistent with recent findings in experimental neurophysiology. Keller[9] dissociated the mechanism of heat loss from that of heat production by a lesion in the brain stem. Beaton, Leininger and McKinley[2] demonstrated dissociation of the same mechanisms. Within the heat loss mechanism they dissociated panting and sweating by means of various midbrain lesions and within the heat conservation mechanism they dissociated shivering and pilo-erection. Magoun[11] has found that it is possible by partial spinal section to interrupt conduction in the spinal facilitatory and suppressor pathways differentially.

The objective evidence of disturbances of vasomotor function after unilateral chordotomy agrees with the clinical findings of Sjöqvist,[16] who observed a marked drop in blood pressure following many unilateral chordotomies. It is well established that bilateral chordotomy may lower the blood pressure. However, it has not been appreciated that a similar effect may follow unilateral chordotomy.

In a case previously reported[8] in which orthostatic hypotension followed bilateral chordotomy, it was found that after 6 months, cutaneous vascular responses to heating were normal while the orthostatic hypotension persisted. This accords with work by Verel[18] and by Stead and Ebert[17] which suggests that there are at least two types of vasoconstrictor reflexes and that one type may be impaired without the other being affected.

It is probable that autonomic pathways run in other than the anterolateral columns in man. Experiments on animals indicate that this is true. However, Oliver's[12] work in sectioning the lateral columns, and that of Putnam,[13] would suggest that autonomic fibers are not carried in the lateral columns of the cord.

It is apparent that the autonomic pathways are more widely distributed

in the cord than has been thought and that the greater part of them are not intimately related to the pyramidal tract. There was no evidence of injury to the pyramidal tract in any of our cases.

SUMMARY

Disturbances of vasomotor function occur after unilateral chordotomy as well as after bilateral chordotomy. Vasomotor and sudomotor function may be dissociated by lesions in the anterolateral quadrant of the spinal cord. The autonomic fibers are more widely distributed in the anterolateral column of the spinal cord than has been thought.

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THE USE OF REFRIGERATED AUTOGENOUS BONE FLAPS FOR CRANIOPLASTY

GUY L. ODOM, M.D., BARNES WOODHALL, M.D., AND FRANK R. WRENN, JR., M.D.

Division of Neurosurgery, Department of Surgery, Duke University School of Medicine, and Duke Hospital, Durham, North Carolina

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THIS report concerns experience with the use of frozen autogenous bone flaps for delayed cranioplasty. The use of frozen autogenous bone fragments for the repair of cranial defects has previously been reported by Elliott and Scott.[3]

We report 6 cases in which it was necessary on 7 occasions to remove the bone flap because of cerebral swelling. In all 7 instances, the osteoplastic technique had been used to enter the skull. The pericranium was stripped away from the flap and left attached to the integument. No special effort was made to reconstruct continuity of the pericranium. The scalp was closed in routine fashion in layers. Upon removal, the flap was wrapped sterilely in dry gauze and a towel, labelled, and stored in a deep freeze unit maintained at minus 4.0°C. After varying intervals the flaps were reinserted as delayed autogenous free grafts. Each case has been followed clinically and with serial x-rays of the skull.

Case 1. P. B. (D.H. B–638) was operated upon in March 1943 and in two stages. On the first occasion a large parasagittal meningioma was exposed through a mid-parietal flap which was removed and refrigerated. Excessive vascularity leading to free hemorrhage from the tumor influenced the decision to stage the procedure. Ten days later the tumor was removed and the flap replaced.

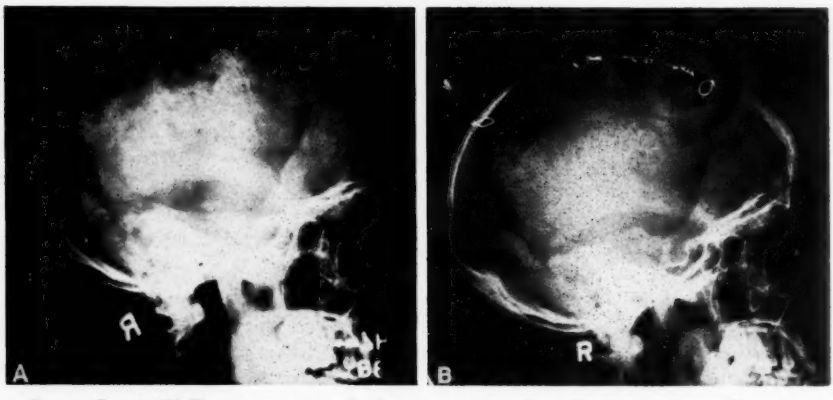

FIG. 1. *Case 1.* (A) X-ray appearance of a frozen autogenous bone flap 1 year after replacement. (B) Approximately 8 years after replacement.

The postoperative course was entirely uneventful. One year later there was x-ray evidence of bony union along the medial edge of the flap (Fig. 1A). However, at this time mottling indicated some central absorption. Eight years postoperatively the patient was essentially asymptomatic. The bone flap appeared firmly united on palpation. X-rays revealed evidence of firm union along the anterior and posterior edges. The previously mottled areas had increased in density and practically disappeared (Fig. 1B).

Case 2. M. L. (D.H. C-11962) had a right frontal craniotomy for glioblastoma. To facilitate a subsequent biopsy in the course of attempted chemotherapy of the tumor, the flap was removed and refrigerated. Two weeks later it was replaced.

The postoperative course was uneventful. Four months later the patient was readmitted. X-rays of the skull revealed slight absorption about the suture wires but otherwise no definite changes. There was little x-ray evidence of union. Progression of tumor growth necessitated sacrifice of the flap for decompression 4½ months after insertion. When operatively exposed the flap was found to be firmly united requiring removal with the Gigli saw. The flap was observed to be extremely vascular with abundant evidence of vascular ingrowth. Save for some thinning of the diploe the appearance was not remarkable.

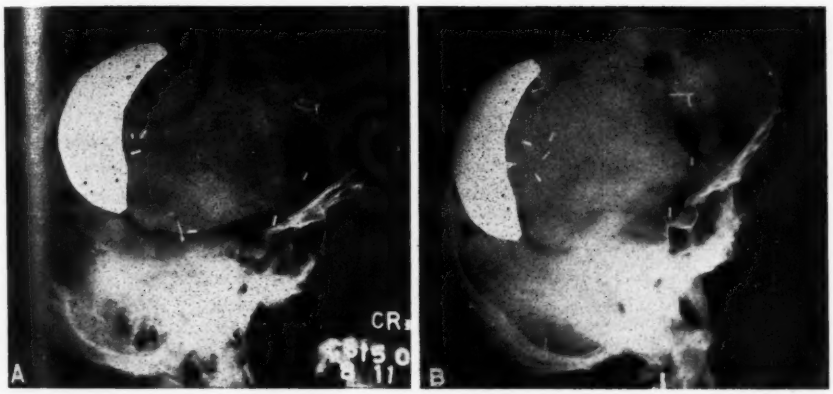

FIG. 2. *Case 3.* (A) Roentgenogram of a frozen autogenous bone flap 1 week after replacement. (B) Appearance 31½ months after cranioplasty.

Case 3. J. W. (D.H. C-61509) was subjected to a right temporal-occipital craniotomy for parasagittal meningioma. Because of cerebral swelling the bone flap was removed and refrigerated. One week later it was replaced and a small piece of tantalum was added to completely cover the bony defect (Fig. 2A).

Postoperatively small amounts of serosanguineous fluid were aspirated from beneath the scalp flap, but otherwise the course was smooth. He was readmitted 22½ months later for progressive mental confusion of 3 months' duration. X-rays of the skull revealed firm union with little or no absorption. At this time there was evidence of tumor on the opposite side and additional meningioma was removed through a left craniotomy. At operation the flap in place on the right was found to be firmly united. It was necessary again to refrigerate the bone flap. Roentgenograms

31½ months after replacement showed continuing union of the right flap with little evidence of absorption (Fig. 2B). At this time the left flap refrigerated for 9 months was replaced. Biopsy of the right flap and the adjacent intact skull was obtained at this time.

Case 4. B. P. (D.H. C-81547) had a left occipitoparietal craniotomy with removal of a large subdural hematoma. The postoperative course was troubled. He remained drowsy and became progressively unresponsive and 24 hours after operation the wound was reopened and a postoperative extradural hematoma was removed with immediate improvement. Twenty-four hours later he was again unresponsive and fluid was aspirated from beneath the scalp flap. This was repeated on several occasions with but little improvement. Seven days after the original craniotomy the bone flap was removed and refrigerated. Recovery was now uneventful and rapid.

Six months later the bone flap was replaced. Wound healing was prompt. The patient was without complaint 6½ months later. X-rays now revealed slight absorption along an edge of the flap and no evidence of union.

Case 5. W. C. (D.H. A-27806) had an occipital lobectomy for ependymoma through a left occipitoparietal craniotomy. Presence of cerebral swelling necessitated removal and refrigeration of the bone flap.

An autogenous bone flap cranioplasty was carried out 11 months later. The postoperative course was smooth. Roentgenograms 5½ months later showed union along the edges with slight central absorption; 17 months later union was firm about the edges but there was slight absorption still apparent.

Case 6. S. J. (D.H. C-80990) had a right parieto-occipital craniotomy with ligation of large feeder vessels to an arteriovenous angioma. Cerebral edema necessitated storage of the flap in the deep freeze. After 1 week the flap was replaced. The postoperative course was uneventful.

At 15 months there was still no evidence of union roentgenographically. However, there was little evidence of absorption and the flap appeared firmly fixed and the scalp was well healed.

DISCUSSION

There have been no failures when refrigerated bone was used for cranioplasty. In this series the refrigeration period varied from 10 days to 11 months. Prompt clinical wound healing without excessive fluid collection or foreign-body reaction was the rule. Serial x-ray studies reveal an initial mild absorption, particularly at the edges of the flap, during the first few months which may gradually increase through the period of a year. After this time the x-ray density increases towards uniformity. Clinically union has always been firm from the time of immediate wound healing. Verification of the gross occurrence of bony union was found 4½ months after cranioplasty in 1 case. Further evidence for bony union appears in the microscopic sections of biopsy material taken 31 months after cranioplasty. The temporal arrangement of healing resembles closely that reported by others with free bone flaps immediately replaced without physical treatment.[1,7]

In 4 additional cases, after removal from the freezer, the flap was boiled in the autoclave for 10 minutes prior to reinsertion. In 3 of the 4 instances it has been necessary to remove the flap. In 2 cases the flap was removed after

5 weeks and 8 months respectively because of infection following scalp aspiration present at the time of original removal. In the third case failure was engendered by progressive absorption occurring in a 9-year-old boy (Fig. 3). This flap was removed after 5 months.

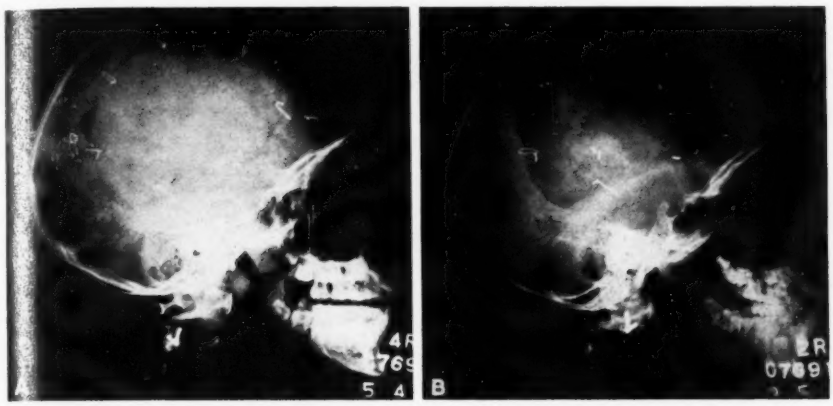

FIG. 3. Demonstrating marked absorption observed in a frozen autogenous bone flap boiled for 10 minutes prior to replacement. (A) Immediate postoperative film. (B) Appearance at 5 months.

In the fourth case there has been persistent drainage of serosanguineous material from a small sinus in the scalp, and the x-ray demonstrates a degree of absorption far exceeding that shown by flaps that have not been boiled.

This experience with boiled bone flap replacement parallels the experience of others. Thus, Naffziger, recording a portion of his early experience in 1935 noted absorption in boiled free bone plates.[5] Ray and Parsons found it necessary to remove 4 of 11 flaps subjected to boiling for reasons of excessive absorption and apparent infection[7]. They suggested that boiled flaps were more satisfactory if replaced immediately, as in techniques for treatment of bony tumors of the skull, than when replacement was delayed. We suggest that combined refrigeration storage and subsequent boiling may place the flap in double jeopardy and should probably be avoided.

We are not prepared to enter the controversy as to whether the refrigerated bone remains viable or simply serves as a trellis for the ingrowth of new bone from the adjacent structures. The consensus of various workers is that the latter idea obtains for long bone grafts.[2,4,6] Our few microscopic studies provide no adequate answer. In a single biopsy specimen obtained 31½ months after replacement (Fig. 4) the marrow of the graft is fibrotic, but revascularization and cellular activity is evident in the Haversian system. This suggests the concept of healing by "creeping substitution."

Regardless of the question of viability the refrigerated autogenous bone flap grafts appear most satisfactory for covering cranial defects. The replacement of such flaps is a safe, simple procedure yielding the best cosmetic result and we believe that the method when feasible is superior to other methods of cranioplasty involving the use of inert metals or plastics.

FIG. 4. Section through the line of union of an autogenous bone flap in place 31½ months. Note the fibrotic marrow, but evidence of revascularization in the flap which is to the right.

SUMMARY

Replacement of refrigerated autogenous bone flaps removed 10 days to 11 months previously has been carried out 7 times in 6 cases. Results have remained satisfactory for periods of 6 weeks to 9 years in all instances.

Three of 4 refrigerated autogenous flaps boiled 10 minutes prior to replacement have been subsequently removed because of marked absorption or infection.

When feasible it is believed that refrigeration of the bone flap upon its removal and its subsequent replacement is superior to other methods of cranioplasty made necessary if the flap is sacrificed completely.

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ON THE ANATOMY OF ANTEROLATERAL CORDOTOMY*

EDGAR A. KAHN, M.D., AND ROBERT W. RAND, M.D.
Department of Surgery, Section of Neurological Surgery, University Hospital, Ann Arbor, Michigan

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THE fact that prefrontal lobotomy is being used with increasing frequency in cases in which a properly performed anterolateral cordotomy would suffice for the relief of intractable pain, is to us an indication that the exact technique of the latter procedure is still not common knowledge.

Prefrontal lobotomy is a definite contribution to the control of pain but it is as yet not a precision operation and the results are consequently unpredictable. It is now accepted that more obvious personality defects arise when the procedure is used for pain than for psychosis. Consequently the relief of pain is sometimes obtained at the price of a change of character in the patient which is most distressing.

In general, we believe that when pain can be controlled by a properly performed root or tract section, lobotomy should be held in abeyance. An exception to this rule is when life will still be intolerable following the relief of pain because of severe apprehension or some unsightly ulcerative deformity. Here lobotomy may be the operation of choice.

In 1937 the conclusion was reached in this clinic[3] that in order to obtain high levels of analgesia that would persist, the incision had to be carried not just to the anterior nerve root but from 1 to 2 mm. anterior to it. This was later confirmed by Hyndman and Van Epps[2] and by Walker[6] in man, and by Weaver and Walker[7] in the monkey.

Cordotomy patients are notoriously difficult to follow postoperatively since the majority die in nursing homes at a distance from the neurosurgical clinic. In a necessarily incomplete check-up study in 1948, we were surprised to learn that many of our patients were still not obtaining complete relief of pain or were having recurrence. It was then suggested that the incision be carried invariably 2 mm. anterior to the anterior nerve root.[4]

In the past 3 years 63 patients have undergone anterolateral cordotomy on the ward service. Many of these operations were carried out by residents usually supervised by the senior author who insisted on their demonstrating an incision into the cord substance anterior to the anterior nerve root. In all but 1 case a satisfactory upper level of analgesia was obtained, though in several instances it was not higher than the 11th dorsal segment. In only the 1 case was it necessary to re-operate to obtain a higher level of analgesia,

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in spite of the fact that these procedures were all carried out under general anesthesia.

In 4 cases, however, the saddle or leg area was spared on one side, or normal sensation returned to it within a few days, the recurrence of pain necessitating re-operation. The avoidance of this particular error constitutes the basis for the following discussion, for cordotomy is a precision operation. The procedure should not be condemned if a poor result follows faulty technique.

CASE REPORTS

Case 1.—A 38-year-old negro woman had been treated for medullary squamous cell carcinoma of the cervix in 1947–48 by total hysterectomy and x-ray therapy. Six months prior to admission to the University Hospital increasingly severe pain developed in the low back and right leg.

Examination. A hard mass of nodular outline filled the right pelvis. A hard supraclavicular node was present on the right, biopsy of which revealed metastatic neoplastic tissue.

1st. Operation. Cordotomy was performed on June 22, 1950, the left side being sectioned first. Before the right side was cut the patient became hypotensive.

Course. The following day the level of analgesia was at the 4th thoracic segment on the left and the 9th on the right. This patient had had an irradiation vesicular reaction on the buttock as a result of further x-ray therapy given 2 months prior

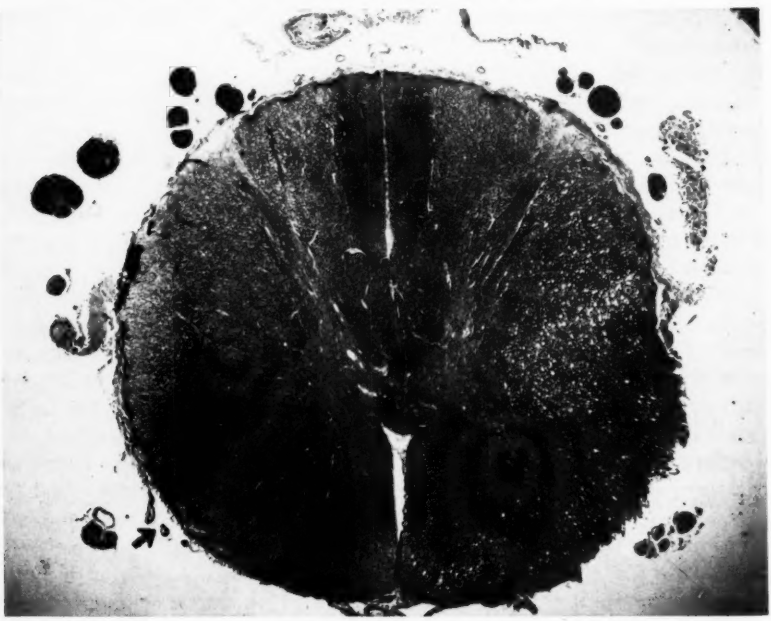

FIG. 1. Cordotomy at C3 cord segment. Arrow points to center of anterior nerve root. There has been some damage to "caudal" rubrospinal tracts; clinically there was no paralysis.

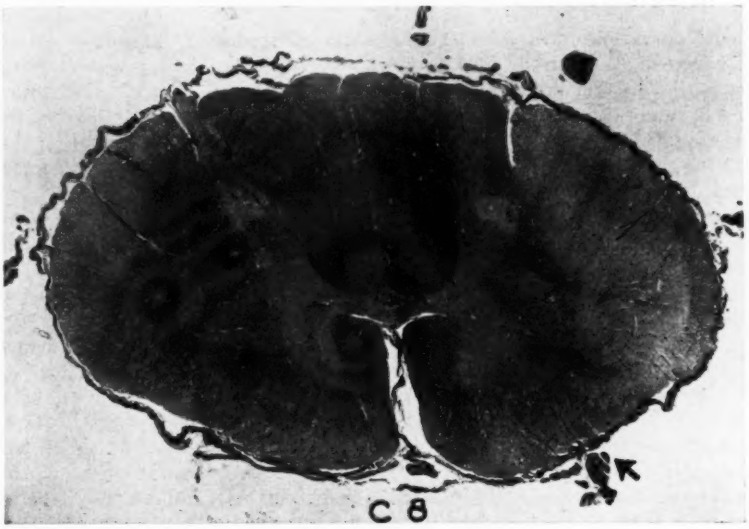

FIG. 2. Nearness of anterior nerve root to anterior spinal artery seen in normal spinal cord at C8. This relationship is maintained throughout cervical enlargement.

to admission. On the 3rd postoperative day she stated she was having pain and burning in the left gluteal region. Examination revealed normal sensation in the sacral segments on the left although she still maintained her level to T4 on the trunk.

2nd Operation. On July 6 the wound was re-opened. Inspection of the cordotomy incision on the right revealed that the incision had not been carried back to the dentate ligament probably because of a prominent blood vessel over the spinal cord substance at that point. The intact area between the dentate ligament and the cordotomy incision was approximately 1 mm. in length. The knife was now inserted to a depth of 3 mm. severing only those fibers that had been spared inadvertently just anterior to the dentate ligament. Further anterior and medial incision was purposely not made, so that the only new section at this operation was in the posterior portion of the lateral spinothalamic tract.

Postoperative Course. There was complete saddle anesthesia and the patient was relieved of pain without increase in weakness of the lower extremities, though incontinence was present. She was discharged to a nursing home but no subsequent information could be obtained.

Case 2.—A 43-year-old white female was admitted on Aug. 31, 1950, because of intractable pain in her left hip and leg of 4 months' duration. X-rays of the pelvis revealed neoplastic destruction of the left acetabulum, ilium and pubic bones. Chest and lumbar spine x-rays were normal. In 1948 she had been treated for squamous cell carcinoma of the cervix, grade III, with deep x-ray therapy.

Examination. The general physical and neurological findings were normal except for some generalized swelling of the left leg, tenderness over the left hip, and slight quadriceps muscle weakness on that side.

1st Operation. On Sept. 5, 1950, a bilateral high dorsal cordotomy was performed. The cordotomy knife was set at 4.5 mm. and inserted into the spinal cord on the right approximately at the 2nd thoracic segment. The incision was started just beneath the attachment of the dentate ligament with the cord. The knife was angled 15° inferior to the horizontal plane of the cord and brought out 2 mm. medial to the anterior nerve rootlets. A similar procedure was then performed on the left side at the 3rd thoracic spinal cord segment. The 2nd posterior root on the right was crushed.

Course. On the 5th day pain slowly recurred in the left leg. The pain became as severe as it had been pre-operatively. Daily examinations up to that time had revealed complete analgesia below the 4th thoracic dermatome segments bilaterally; deep pain to Achilles tendon pressure had also been absent. By the 7th postoperative day, although the thoracic level of analgesia was unchanged, pain to deep pressure of the Achilles tendon* had returned and there were scattered skin areas sensitive to superficial pain over the posterior aspect of the left thigh and calf.

2nd Operation. Re-exploration was performed on September 12. On the right side it could be clearly demonstrated that the incision extended 2 mm. anterior to the anterior nerve rootlets, but there was a normal area, about 1 mm. in length, between the attachment of the dentate ligament and the dorsal extent of the incision. The cordotomy knife was inserted through this area and directed as had been done previously but to a depth of only 3 mm. The incision was now inspected on the left and it was seen to start exactly at the attachment of the dentate ligament and to extend 2 mm. anterior to the anterior nerve rootlets.

Course. The patient was discharged 4 weeks later, ambulatory and completely relieved of pain. The level of analgesia remained at the 4th thoracic dermatome with complete loss of superficial and deep pain sensation below this level.

She was re-examined 2 months postoperatively with the same neurological findings. No indwelling catheter was necessary. She was entirely free of pain up to the time of her death Dec. 4, 1950.

Case. 3.—A 63-year-old white female was admitted on Nov. 28, 1950, for severe recurrent right leg and back pain. The patient had been discharged from the hospital 2 months previously following a decompressive lumbar laminectomy and posterior rhizotomy of the 2nd and 3rd lumbar roots on the left for relief of cauda equina compression. This was secondary to a pathological fracture of the 2nd lumbar vertebrae from a leiomyosarcoma of the uterus.

Examination. Positive findings were hypesthesia over the distribution of the 2nd and 3rd lumbar dermatomes on the left and minimal weakness of the right leg. A chest x-ray revealed two to three small pulmonary metastases.

1st Operation. Because of her very severe radicular right leg pain, a high dorsal cordotomy was performed on Nov. 30, 1950. The knife was believed to have been inserted on the left just at the dentate ligament attachment to a depth of 4½ mm., emerging 2 mm. anterior to the anterior nerve root. A similar procedure was carried out on the right. The 2nd thoracic posterior nerve roots were crushed.

Postoperative Course. There was complete relief of pain for the first 5 days, and

* If pain can be produced by pressure over the Achilles tendon following anterolateral cordotomy it is quite certain that pain fibers from sacral segments have been preserved in the lateral spinothalamic tract.

Yoss[8] has shown in the monkey that a lesion in the most dorsolateral portion of the lateral spinothalamic tract prevents painful stimuli to the exposed contralateral Achilles tendon from reaching consciousness.

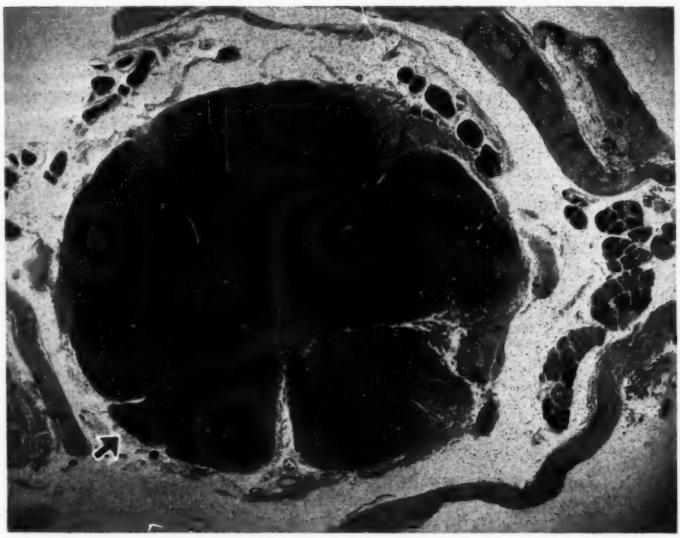

FIG. 3. Ample cordotomy between D2–D3 spinal cord segments with analgesia to D5–D6 dermatomes.

the level of analgesia remained, bilaterally, at the 4th thoracic dermatome. On the 6th day recurrent pain developed in the posterior aspect of her right leg which became progressively more severe. The saddle area remained analgesic but temperature and pain sense was present about the right ankle as well as pain to deep pressure of the right Achilles tendon. The left leg remained analgesic.

2nd Operation. On Dec. 13, 1950, the cordotomy was revised. On inspection of the left cordotomy incision it was seen to start 1 mm. anterior to the dentate ligament rather than exactly at the attachment. It could be shown to extend at least 2 mm. anterior to the anterior nerve rootlets. The cordotomy knife was reinserted into the incision at the dentate ligament attachment and directed as was done previously at a 15° angle to the horizontal level of the cord, but only to a depth of 3 mm. The section made on the right side was next examined and found to start at the junction of the dentate ligament with the cord, and to extend 2 mm. anterior to the anterior nerve root.

Course. The patient was somewhat hypotensive for the first 2 postoperative days but had complete relief of pain in the right leg with loss of pain sensation to pin prick or deep Achilles tendon pressure. On the 3rd postoperative day there suddenly developed complete peripheral vascular collapse and she died. No autopsy was obtained.

Case 4.—A 51-year-old negress was admitted on Nov. 29, 1951 because of severe lower abdominal pain secondary to far advanced carcinoma of the cervix. In July she had received extensive irradiation treatment for this condition. There was a vesicovaginal fistula present.

Examination. Neurological findings were normal. X-rays of the chest and pelvis showed no pulmonary nor osseous metastasis.

1st Operation. On Dec. 5, 1951 a high bilateral dorsal cordotomy was performed at approximately the 2nd thoracic spinal segment on the left and the 3rd segment on the right.

Postoperative Course. The level of analgesia was at the 6th thoracic dermatome on both sides. The patient was free of pain until the 5th postoperative day at which time she complained of recurrent lower abdominal pain. The upper levels of analgesia were unchanged. Sensation to deep and superficial pain was absent on the left but present on the right below the 9th thoracic dermatome, pain sensation becoming more acute as the sacral segments were approached.

2nd Operation. On the 5th postoperative day a revision of the cordotomy was performed. On the left side it was evident that the incision started 1 mm. anterior to

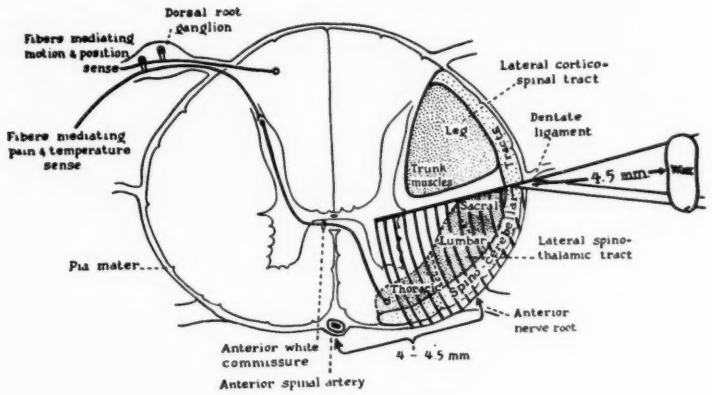

FIG. 4. Ideal cordotomy at upper dorsal spinal cord segments.

the attachment of the dentate ligament to the cord. This area was sectioned by inserting the knife approximately 3 mm. in depth. It was clearly evident that the previous incision extended 2 mm. anterior to the anterior roots and, therefore, the knife was not carried in an anterior direction.

Course. Shortly after this operation the patient was ambulatory. The levels of analgesia remained at the 6th thoracic dermatome below which there was complete loss of sensation to superficial and deep pain. This patient died 3 weeks after discharge from the hospital.

DISCUSSION

Hyndman and Van Epps made an important contribution to the anatomy of anterolateral cordotomy when they showed in man that "fibers representing the lower segments (of the spinal cord) are situated posteriorly in the (spinothalamic) tract and fibers representing successive segments upward dispose themselves more and more anteriorly." They demonstrated that it was possible to produce analgesia over the chest and abdomen without including the lower extremities.

It was their opinion, at the time based on 6 cases, that the region extending 2 mm. anterior to the dentate ligament contained no fibers conducting sensations of pain and temperature. Though there is undoubtedly some anatomical variation, the 4 cases we have reported disprove this conclusion. Walker had concluded before us that sacral fibers "may be spared in dorsal or cervical antero-lateral chordotomy in which the incision is made 1 to 2 mm. anterior to the dentate ligament". We believe, consequently, that when the pain is pelvic in origin the knife should enter the upper thoracic cord exactly at the attachment of the dentate ligament and not "just in front of the dentate ligament" as we had said in a previous communication.

It should be remembered that between the anterior extent of the pyramidal tracts and the posterior extent of the lateral spinothalamic tracts is a zone of white matter that contains the lateral tectotegmental and tegmentospinal ("caudal" rubrospinal) tracts. This constitutes a narrow but important "safety zone" during the performance of an anterolateral cordotomy, as the tracts within this zone can be divided without apparent detriment to the patient, provided the pyramidal tract is not grossly injured. In order to insure avoidance of injury to the lateral corticospinal tract, the cordotomy knife is started at the attachment of the dentate ligament and directed at an angle not less than 15° inferior to the transverse diameter of the spinal cord. To attain high levels of analgesia the tip of the knife should be carried to a depth of 4 to 5 mm. and brought out 2 mm. anterior to the emergence of the anterior nerve rootlets (Fig. 4).

There are several points that might be worth while mentioning in insuring that the incision be made exactly at the attachment of the dentate ligament. First, the dural attachments of the dentate ligaments on both sides should be divided before making the first incision into the cord, in order to obtain satisfactory rotation. Rotation will also be aided by completely freeing up both the anterior and posterior nerve roots from the arachnoid. It may be advisable to divide one posterior nerve root near the point of the incision into the cord in order to obtain maximum rotation. This is especially true at upper cervical levels.

Secondly, the exact line of attachment of the dentate ligament is established by direct visualization because the dentate ligament may be but loosely attached to the spinal cord or may be avulsed from it on rotation of the cord. Since traction on the ligament is in a posterior direction in obtaining rotation, the ligament may be avulsed and come to lie over the pyramidal tract without the operator's knowledge. In our opinion this may have been the cause of any resulting weakness of the lower extremities.

In the lower cervical area (cervical enlargement) the anterior nerve roots leave the cord considerably closer to the midline than in the upper cervical and upper dorsal region. This is therefore a dangerous area at which to perform anterolateral cordotomy since the anterior spinal artery could so easily be damaged. In the upper dorsal spinal cord, as Hyndman and Van Epps have said, the anterior nerve roots do not follow the downward direction of

the anterior horns but come off laterally from them so as to reach the surface of the cord "just slightly more than half the distance from the dentate ligaments to the anterior median fissure". We have measured the distance from the center of the anterior nerve root to the center of the anterior spinal artery in the upper dorsal cord of adults and find it to be invariably from 4 to 4.5 mm. circumferentially. This gives a good margin of safety in preventing the point of the knife from injuring the anterior spinal artery. In the cervical enlargement we have found this distance to be as little as 2 mm. so that one could not possibly carry the cordotomy incision here much beyond the anterior nerve root with safety.

We have lately been much better satisfied with the operation of high cervical cordotomy. We combine it with the crushing of the upper three or four posterior cervical nerve roots on the side opposite the cordotomy incision and the crushing or division of the upper two on the side of the cordotomy incision. This not only raises the level of analgesia but results in a painless operative incision which permits getting the patient up so much more rapidly and definitely shortens convalescence.

It is the opinion of Schwartz[5] that in performing cordotomy at or above C2 level, it is not necessary to carry the incision anterior to the anterior nerve root. Lyle French[1] has now done a total of 32 cordotomies at C2 level. It is his opinion, based on operations performed under local anesthesia, that there is considerable variation in the spinothalamic tract. He estimates the cord incision at C2 segment need be carried only to the anterior nerve root, and not beyond it, in from 80 to 85 per cent of the people in order to obtain analgesia to C4. He has had cases, however, in which it was necessary to carry the incision anterior to the anterior nerve root in order to obtain this level of analgesia.

Above the cervical enlargement the distance from the center of the anterior nerve root to the anterior spinal artery varies from 4 to 4.5 mm. Inasmuch as there is no danger of injuring the anterior spinal artery at upper cervical levels provided the incision is not carried more than a millimeter or two anterior to the anterior nerve root, we still believe it to be the proper procedure when operating under general anesthesia.

SUMMARY

1. In performing anterolateral cordotomy at upper dorsal spinal cord levels, the point of the knife should enter the cord exactly at the attachment of the dentate ligament. The incision should be carried to a depth of 4–5 mm. in a plane making an angle of no less than 15° with the transverse diameter of the spinal cord. The point of the knife should be carried 2 mm. anterior to the emergence of the anterior nerve root.

2. At upper cervical spinal cord levels, when the operation is being performed only for pain above the nipple line, the cordotomy incision, 4.5–5.5 mm. in depth, may be started 1 mm. in front of the dentate ligament.

3. The cervical enlargement is a poor place to perform anterolateral cordot-

omy because of: (1) the nearness of the anterior nerve roots to the anterior spinal artery, (2) the danger of injuring important anterior horn cells supplying the upper extremity, and (3) the fact that rotation of the cord is more difficult here.

We wish to express our appreciation to Drs. Jose Bebin and Wolfgang Zeman of the Laboratory of Neuropathology of the Neuropsychiatric Institute of the University of Michigan, for their careful histological preparations.

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SCHISTOSOMIASIS OF THE BRAIN*

FRANCIS A. CARMICHAEL, JR., M.D.,† AND HOWARD S. COWLEY, M.D.‡
Veterans Administration Center, Wadsworth, Kansas

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ALTHOUGH there is much to be found in the literature concerning intestinal and hepatic involvement by Schistosoma japonicum, the reports on cerebral involvement are infrequent. Because of the extreme gravity of complications from this disease, we feel that the members of American medical profession should be aware of it as a neurological differential diagnostic problem in anyone presenting a bizarre neurological picture who has been in an endemic area. That the disease may well assume the roles played by typhoid fever in the Civil War, by influenza in World War I and by malaria in World War II was suggested at a recent meeting of the Society of American Bacteriologists.

HISTORICAL REVIEW

Fujii[28] first mentioned this disease entity in 1847, but it was 42 years later before any cerebral lesions were associated with the disease[65] and not until 1904 was the etiological agent discovered and named by Katsurada.[37] The first autopsy reports on cerebral findings were made in 1905.[58] Presumptive evidence that abnormal neurological reactions in infected patients were attributable to lesions caused by eggs or worms in the central nervous system was initially presented by Houghton[33] in 1910, but not until 1935 was the first report of surgical verification of a cerebral lesion made by Shimidzu,[49] which was followed by similar reports by Edgar[19] in 1936, and Greenfield and Pritchard[29] in 1937. No further cerebral granulomas were verified surgically until Swanson[55] reported the fourth case in 1946. Since that time, 11 instances of operative and microscopic verification of such lesions have appeared in the literature,[14,19,29,31,47,48,49,51,55,62] although others may have been unreported, as Chang and his co-workers[14] referred to 2 cases surgically verified by Sanders, and Watson and his co-workers[62] mentioned 1 case verified by Maltby and Schmidt and 1 by Chasnoff. Hunt and his co-workers[34] reported 1 operative case which, however, was not verified microscopically. Faust[23] mentioned 1 case verified by Palmer.

Many observers have reported on presumptive ectopic cerebral lesions.[10,12,15,17,20,26,36,52,56,57]

Eight authors[3,4,5,23,56,61,65] reported 11 postmortem examinations on

* The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

† 411 Nichols Road, Kansas City 2, Missouri.

‡ Former senior neurosurgical resident, Wadsworth Veterans Administration Hospital, Wadsworth, Kansas.

patients who had exhibited neurological manifestations of the disease and among these only 1 cerebellar and 4 cerebral granulomas were microscopically verified as containing Schistosoma japonicum ova. Perhaps significantly the number of surgical verifications since 1941 overshadows the number of autopsy verifications.

ENDEMIC AREAS

The disease is apparently limited to areas containing a certain species of amphibious fresh water snail known variously as Oncomelania, Katayama or Schistosomophora which presently is the only known intermediate host suitable for the larval development of Schistosoma japonicum in the field.

Known endemic areas include Japan (Honshu and Kyushu Islands), China (especially southern and central), Formosa, Korea, the Celebes and the Philippine Islands of Leyte, Samar, Mindoro and Mindanao.[10,16,24,40,41,43,44,50,54,59,64]

Abbott,[1,2] and Berry and Rue[9] have reported a species of fresh water snail having a wide range of distribution in the United States which is capable of serving as the intermediate host under laboratory conditions. Their medical significance is presently unknown, but one must recall that after World War I Australia was faced with the previously unknown problem of endemic Schistosoma hematobium due to the adaptability of a certain species of one of their native fresh water snails.

ROUTE OF CEREBRAL INFECTION

The route of larval migration was reported by Miyagawa[42] in 1912, and restudied by Faust and Meleney[25] in 1924 whose description of the stage-by-stage development in mammals is classical. However, this deals only with the normal portocaval development and does not embrace the far distant sites of ectopic lesions.

The largest number of proven or presumptive sites of ectopic lesions in schistosomiasis japonica is in the cerebrum. However, the route of cerebral infestation is not clearly understood. Five routes have been theorized and include (a) the valveless vertebral veins or "Batson's circulation";[7,8] (b) migration of the worms outside their normal habitat against the venous blood flow and into collateral vessels with egg deposition on reaching the end venules.[23,29,48,51] It has been shown that worms do migrate out of their normal habitat and the nature of most of the verified cerebral lesions supports this hypothesis, but no worker has explained how the worms reach the cerebral venous sinuses; (c) normal development outside the hepatic-caval system;[23,29] this has been disproven by the studies of Faust and Meleney[25] and Waelsch;[63] (d) the presence of a patent foramen ovale which, although a rational explanation, does not occur with enough frequency to serve as an explanation; none of the 9 autopsy reports on cerebral ectopic lesions mentions the presence of such an anomaly; (e) eggs deposited in the usual sites filtering through the capillary barriers of the liver and lungs into

the general circulation and hence to end arterioles.[58] The objections to this are the facts that reaction is reported only around venules and never around arterioles, and that the cerebral foci are composed of nests of eggs rather than diffuse lesions, although 3 autopsy reports[58,61,65] mention a diffuse process.

PATHOLOGY

On invading the central nervous system an intense reaction follows in both the cerebral vessels in which the organism lodges and in the surrounding parenchyma. This may be caused by blood-vessel occlusion and resultant passive congestive changes, foreign protein reaction, elaboration of a chemical toxin, or any combination thereof.[25]

Shimidzu's[49] description of the microscopic changes occurring in the involved area of the brain in the first case in which operation was performed is typical except that subsequent authors also report the presence of multinuclear foreign body giant cells. The picture is not radically different from the general reactive one that occurs in cerebral abscess or other granulomas, as previously described in detail by one of us (F. A. C.[11]).

No investigators have mentioned any pathologic changes in the cerebral arteries, and none has reported finding an adult worm in the human cerebrum, but all have noted intense infiltration of nearby cerebral veins and degenerative changes in surrounding ganglion cells, as well as walled-off ova inside the low-grade inflammatory mass.

Later in the paper we shall describe surface features of the pia and arachnoid which we believe provide a rather accurate gross pathologic diagnosis at the operating table and which we have not found recorded heretofore.

Most of the reported gross pathological lesions have been unilateral granulomas in the parieto-occipital or parietotemporal areas. There is apparent predilection for the parietal lobe and questionable affinity for the left hemisphere.

COURSE AND SYMPTOMATOLOGY

The course of this disease may be divided into incubative, acute and chronic stages, although these are continuous and thus the clinical signs and symptoms ascribed to each stage may overlap. As the latent period is variable and of unknown duration, symptoms have been reported as long as 4 years after infection.[29]

The symptomatology of lesions in the central nervous system caused by the presence of eggs and the unidentified substance given off by them has been recorded by many authors.[10,12,13,17,22,25,26,32,33,36,40,43,50,53,56,57,60]

During the incubative stage symptomatology simulates many diseases of the regions endemic for Schistosoma japonicum.

In the acute stage neurologic signs and symptoms include headache, delirium, confusion, aphasias, amnesia, convulsions, hyperreflexia, visual disturbance, nuchal rigidity, loss of superficial reflexes and motor weakness

(especially sudden plegias). Usually these occur about 5 or 6 weeks after infection.

As in all diseases, the individual reaction to infection is variable and because the early signs and symptoms vary as to time of appearance and intensity, they may be entirely overlooked. Furthermore, the early symptoms as a rule subside spontaneously. They are never an index to the severity of the infection. It is noteworthy that many cases of cerebral involvement may give no history whatsoever suggestive of primary infection (including the 3 in this report).

In the chronic stage neurological symptoms and signs comprise headache, language dysfunction, sudden motor weakness or paralysis of one or more extremities or Jacksonian epilepsy (usually ushered in suddenly).

DIAGNOSTIC AIDS

During the incubative stage, only a presumptive diagnosis may be made and the history of exposure is the most important point. Leukocytes and marked eosinophilia without anemia may be found in the blood stream.

Important features noted in the acute stage include the history of exposure, eosinophilia in the absence of allergy or other helminth infestation and the presence of ova in the stools, which may be demonstrated by direct smear or other recommended methods.[6,18,25,43,45] Proctoscopy as advocated by Johnson and Berry[35] may yield valuable results, and these workers as well as others[30,38] advise biopsy as it gave positive results before ova could be demonstrated in the stool. Because of possible complications such biopsy should be done with caution.[59] The recognition of the eggs is excellently presented in a paper by Faust.[21] Intradermal and complement fixation tests are valuable adjuncts.[43] Gastroscopic studies are of no diagnostic value.[46] Cerebrospinal fluid analysis is regarded as diagnostically valueless because the ova have become walled off in the granulomatous mass; however, later in this paper we shall report for the first time in medical literature our isolation of the ova from both the spinal and ventricular fluid.

The chronic stage is somewhat more difficult to diagnose because of the variable clinical pattern, the unknown latent period, and the difficulty in obtaining positive laboratory findings. Usually eosiniphilia and fever are absent, and the finding of ova in the stools problematical—the biopsy methods may be superior to fecal examination in the chronic stage. Results of the formol-gel test are variable[26] as are those of the complement fixation and skin tests.

The differentiation between a cerebral granuloma and a neoplasm is difficult and in fact probably only a surmise until operative biopsy is undertaken. Electroencephalography, ventriculography or pneumoencephalography in patients with focal neurologic signs and papilledema may not aid in the differentiation although the ectopic lesions of Schistosoma japonicum usually do not present such large defects in the ventricular system. We have

not encountered any description of the angiographic picture of these lesions although we presume the design would not be specific.

We should like to stress a point made by Tillman[57] and others, that any patient presenting an obscure neurological pattern who has a history of having been in an endemic area should be thoroughly investigated for schistosomiasis.

TREATMENT

Ferguson and his co-workers,[27] Sullivan and Ferguson,[54] and others suggest that prevention of the disease is better than treatment and to this end they advocate the education of persons in and those going into known endemic areas, the application of cercaricidal preparations to the skin and clothing and the wearing of protective clothing by those who must work in suspected surface waters. They emphasize that the criteria of safety are neither the absence of snails nor the presence of clear or swiftly flowing water, pointing out that cercaria may be carried for miles on water surface films.

Because of the gravity of the disease and its complications, students of it[10,16,23,25,32,36,40,43,53,60] advise institution of specific chemotherapy as soon as schistosomiasis has been diagnosed, not only to guard against further complications but also because it is the only efficacious method of removing the parasites. The commonly employed agents are antimony compounds, including stibophen (neoantimosan or fuadin) and antimony potassium tartrate (tartar emetic) which are toxic and dangerous but which should be given promptly unless contraindicated by the presence of another serious disease. They emphasize particularly close observation of the patient and mention that other heavy metal salts and cardiac depressants should not be administered concurrently. It is stressed that insufficient dosage of the drug usually is followed by therapeutic failure. Recent military experiences have demonstrated the superiority of tartar emetic for specific therapy; however, if this drug cannot be tolerated in its maximum recommended dosage, then fuadin should be employed.

Lippincott and his co-workers[39] noted no harmful effect on the liver from antimony given to 2 infected patients who came to autopsy during the treatment of 481 cases.

The results of treatment should be carefully checked, especially by examination of the stools, and the patient should be re-examined frequently for at least 1 year for possible recurrence.

As antimony presumably affects only the adult parasites and has no effect upon the granulomatous lesions, the treatment for ectopic lesions is surgical excision. However, in our Case 3 the ova were identified by cerebral biopsy and in the cerebrospinal fluid, and yet at autopsy multiple lesions were found in the cerebrum but no ova could be microscopically verified although the ova were identified in the preservative solution. Surface lesions can usually be completely removed, intracranial pressure, which in some cases is not only dangerous to vision (50 per cent have papilledema) but also to

life, can be alleviated, and without surgical intervention neoplasm cannot be ruled out with certainty.

PROGNOSIS

Our conclusion on reviewing the literature is that prognosis for life is good. The early cases show much more favorable response to specific therapy than do the latent cases. Mild to severe neurologic residuals may be expected in most of the operated latent cases for at least 1 year.

CASE REPORTS

Herewith follows the report of 3 surgically verified cases, 2 with gratifying results and 1 terminating fatally. We shall describe certain gross pathological findings and laboratory phenomena which have not heretofore received notice.

Case 1. A 30-year-old white male, a packing house worker, was admitted to the hospital on June 28, 1948, complaining of periods of inability to speak and a recent convulsive seizure.

In December 1947 while at work he noted a burning sensation in the right buttock and involuntary movements of the right leg, following which he was unable to move the leg. This phenomenon lasted approximately 5 minutes, after which he felt perfectly normal. During the next 2 weeks, he had four similar attacks and was then symptom free until about 1 month prior to admission when he began to experience headaches and visual difficulty.

On June 23, 1948, he first noted inability to speak although he was able to understand what his fellow worker was saying. This lasted 20 minutes. The same afternoon he had a similar attack of motor aphasia which was accompanied by weakness and Jacksonian convulsive seizure, which began in the right hand and became generalized, with loss of consciousness. There was no tongue biting or incontinence. The unconscious period lasted 1 hour following which he was unable to speak for 15 minutes. He felt well except for a slight pressure behind the left ear. On June 26, another bout of motor aphasia occurred, lasting 20 minutes. On the day of admission, he experienced another attack of similar duration and character.

Past History. His past civilian medical history was not contributory. His military history from July 1942 until January 1946 consisted of 31 months of service in the Southwest Pacific, 6 months of which were spent on the Philippine Island of Leyte. He recalls no illness except mild diarrhea which he thought everyone had at one time or another during their Pacific tour. This caused him no loss of time from his duties.

Examination. The patient was fairly well developed and well nourished and did not appear ill. Positive neurological findings were lateral nystagmus, more pronounced on looking to the right; slight left central type facial weakness; generalized hyperreflexia, more marked in the deep reflexes on the right, especially in the upper extremity; slightly impaired stereognosis on the right and an associated weakness in the right grip. Tentative diagnosis: expanding intracranial lesion in the left parieto-occipital area.

Initial laboratory studies revealed an eosinophilia of 14 per cent, and a leucocytosis of 14,000/c.mm., with 60 per cent neutrophiles and 24 per cent lymphocytes. X-rays of the chest, skull sinuses and mastoid were reported as normal. EEG was reported as evidencing a disturbance in the left parieto-occipital region. CSF

pressure was 180 mm. on the conventional water-type manometer. Pneumoencephalography was done, with fractional displacement of 120 cc. CSF with air. The films evidenced some flattening of the posterior horn of the left ventricle.

On July 9, 1948 the patient was seen for the first time by one of us (F.A.C.), who, concerned by the diagnosis of an expanding intracranial lesion, suggested the possibility of cerebral schistosomiasis and recommended further laboratory examinations. The 15th stool specimen was reported as being positive for the presence of the ova of Schistosoma japonicum.

Operation. On Aug. 6, 1948, a left osteoplastic parietal craniotomy was undertaken. Immediately underlying the dura numerous fine, small, punctate granular adhesions, yellowish-white in color and the size of millet seeds, were encountered all through the pia. Such clusters were adherent to the overlying dura mater and were separated with some difficulty by cotton pledget dissection. Remnants of these clusters could be seen attached to the internal surface of the dura. Palpation of the brain in the posterior parietal area gave a sense of density immediately underlying the cortex. Therefore, incision was made in one of the postparietal convolutions; exploration revealed very dense granulomatous tissue, which was ill circumscribed and not clearly defined from the rest of the brain in this area. A block dissection was made, following which the cut surface of the granuloma could be readily recognized. Several smaller granulomas were removed by blunt dissection and the electric loop.

Pathological Report (Dr. Ferdinand C. Helwig). Granuloma of the brain containing ova of Schistosoma japonicum.

Course. Postoperatively transitory right-sided weakness, confusion and aphasia were noted. All symptoms subsided by the 6th postoperative day.

On August 19, blood serum was submitted for complement fixation test, at which time skin-testing antigen also was employed. It was subsequently reported negative and the skin test read as positive. At this time specific tartar emetic therapy was begun. Stool specimens continued positive for Schistosoma ova until August 31, following which the stool specimen taken every 3rd day was reported negative for parasites or ova. The specific therapy was completed on September 24 and the patient was subsequently discharged. Neurological and eye findings were normal.

Neurological and laboratory examinations every 3 months in 1948 and 1949, and every 6 months since show him to be well and without evidence of further infection. He was last examined in May 1952.

Case 2. A 27-year-old farmer was admitted on Sept. 8, 1948 complaining of headache, failing vision, and clumsiness and weakness of all extremities.

He had been in good health until October 1947, when he first noted flashes of light before his eyes, which he described as being like a neon sign flashing on and off, and difficulty with close vision. This phenomenon would last for several minutes and was followed by severe occipital headaches of variable duration. Usually, however, the headaches lasted for several days, with only partial relief on rest and prescribed medications. They became progressively worse, and since May 1948 had been constant. He no longer experienced visual phenomena but was unable to read because of failing vision. During the last month, he had had progressive difficulty in gait; he could not walk without staggering, preponderantly toward the left. For 4 months he had also noted progressive clumsiness of the upper extremities, especially marked in the last 6 weeks. For several months he had had difficulty in thinking

and expressing himself. He would often say the wrong words, would be unable to complete sentences, and could not figure out small problems. There had been no nausea or vomiting, no diplopia, and no convulsions.

Past History. His past civilian medical history was not contributory. His military history from October 1942 to December 1945 included 13 months spent in the Southwest Pacific on Leyte, Mindoro, and Mindanao Islands. During his service on Mindoro, he was hospitalized for about 1 week with what was diagnosed as dengue fever. He also admitted to several episodes of diarrhea.

Examination. He was a fairly well developed and well nourished white male who was ambulant on a very wide base. All movements were accomplished very slowly and deliberately. He was completely oriented but had some difficulty in cerebration as well as speech and seemed to grope for words, his speech being slow and somewhat slurred.

There was tenderness to percussion over the calvarium in the left occipital area. Kernig plus nuchal rigidity was present. Lateral nystagmus was noted. There was bilateral papilledema of 1D. Confrontary visual fields suggested a right inferior quadrantanopsia. A flattening of the skin of the left forehead was noted on attempting to raise the eyebrows; however, both the patient and his wife believed this had been present for several years. There was difficulty in movements of the tongue and mild fibrillation was noted. The plantar response was equivocal. There was generalized hyperreflexia. All extremities were mildly spastic and voluntary movements were carried out very slowly, more difficulty being noted on the right. No sensory disturbances were elicited. There were dysmetria and dysdiadokokinesis of both upper extremities, more marked on the right. Ataxia was marked, especially in the right leg. The Romberg was very positive, with the patient falling to the left.

Routine laboratory findings were normal except for elevation of sedimentation rate to 31 mm./60 min., and 5 per cent eosinophils in the differential leukocyte count. The stool specimen was reported positive for the presence of hookworm and whipworm. Roentgenograms of chest and skull were normal. The EEG indicated a focal lesion in the left occipitotemporal area.

Operation. On Sept. 17, 1948 ventriculography was performed. The ventricular fluid showed a total protein of 95 mg. per cent; smear, culture, cell count and serology were normal. During the procedure a hard firm mass was encountered under the left occipital burr hole. A biopsy of this mass was reported as protoplasmic astrocytoma. Previous ventriculograms had shown definite asymmetry of the ventricular system, with the left lateral ventricle being depressed somewhat downward, especially in the posterior horn.

A left osteoplastic flap was reflected to expose the left occipital pole. Incision of the dura at the most superior exposure of the cortex showed the color of the tissue to be rather brown and greenish. As the dura was reflected from the pia, a multitude of small, yellow, glistening discrete millet seed-like dots in clusters were seen forming adhesions between the dura and the underlying arachnoid. (The operator remarked at once that these were identical to the clusters of ova of Schistosoma recently seen in a previous case.)

Exploration with the cannula revealed a very hard, tough tumor mass underlying all the occipital cortex at a depth of less than 1 cm. Incision was then made in the occipital cortex and piecemeal removal of the mass was begun. The tumor, except for its large nutrient and traversing arteries, was mainly avascular. It presented

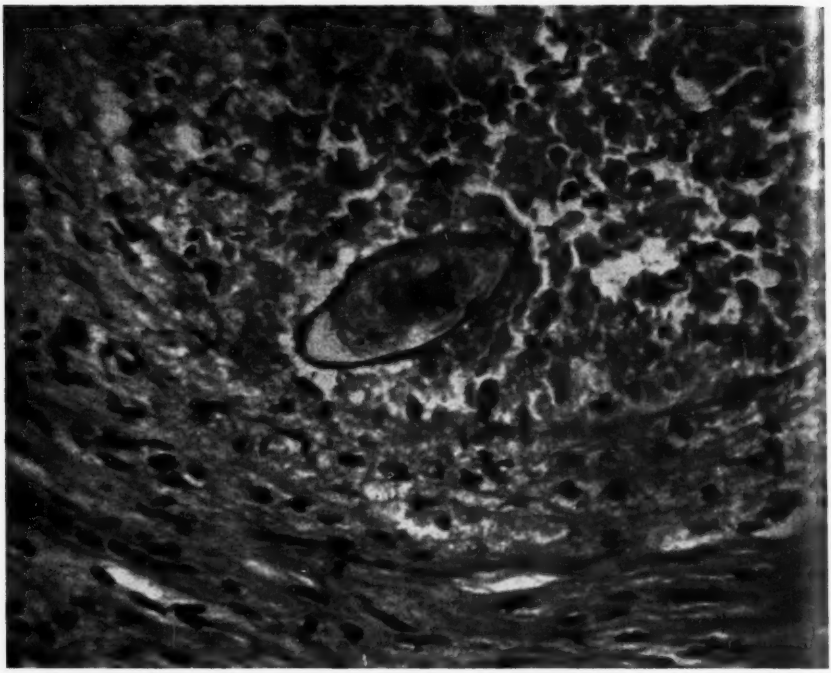

FIG. 1. *Case 2.* High power appearance of a Schistosoma ovum lying between the central necrotic area and the surrounding fibrous zone of a chronic granuloma. (Hematoxylin and eosin, ×900)

a tough, yellowish, avascular, granulated surface when cut with the Bovie or with the scalpel. Extensive dissection of the uncircumscribed tumor mass was done, at which time it was appreciated that tissue approximately 6 cm. in diameter had been removed and that an equally large portion seemed to extend forward toward the mid-parietal lobe and that it was intimately connected with the torcular angle. It was thought most advisable to close and give the patient a course of tartar emetic therapy before considering the advisability of re-exploration for total removal.

Pathological Report (Dr. Ferdinand C. Helwig). Granuloma of the brain, containing Schistosoma japonicum ova (Fig.1).

Course. On September 25, skin and complement fixation tests were done. The skin test evidenced a suspicious positive and the complement fixation test was positive for schistosomiasis.

On September 27, examination by the eye department disclosed blurring of the disk margins, which they assumed to be postpapilledemic, and a right homonymous hemianopsia.

Daily stool specimens continued to be negative for the presence of Schistosoma ova, and continued so throughout the period of hospitalization. However, specific tartar emetic therapy was begun. Sigmoidoscopic examination carried out in search for lesions proved negative.

Examination prior to discharge revealed visual defects as mentioned. Cranial

nerves were intact and there was no longer an ironing-out of the left forehead on raising the eyebrows. There was generalized hyperreflexia with no pathological reflexes or sensory disturbances. During his convalescence he had complained of two transitory bouts of flashing lights.

Subsequent physical and laboratory examinations every 3 to 6 months to May 1952 paralleled the discharge findings. He is able to continue his farming activities satisfactorily.

Comment. Ova were never demonstrated in this patient's stools despite the unquestioned finding of ova in the cerebral granuloma.

Case 3. A 30-year-old butcher was seen in consultation by one of us (F.A.C.) on Mar. 7, 1949, complaining of a feeling of numbness over the entire right side of the body including the face, slowing of all his muscular movements, staggering gait, and some slurring of speech. He gave a history of occasional spells of uncontrollable jerking or twitching in the right arm and leg, followed by severe headache over his right eye and tiredness, which began about November 1948. Examination revealed lateral nystagmus, more marked on the right, dysarthria, dysmetria and adiadokokinesis on the right, a positive Romberg, ataxic gait, sluggish abdominal reflexes, and a suggestion of increased reflexes in the right lower extremity. He exhibited a right hemiparesis including the face, and a subjective right hemihypesthesia. Diplopia was noted on lateral vision toward the right. Admission to the hospital was advised.

Past History. His service medical history from Dec. 14, 1942 to Feb. 18, 1946, included 2 years of overseas duty, 8 months of which were spent in Luzon and Korea. He recalled no bouts of illness except diarrhea, which he described as mild. The patient had been hospitalized elsewhere on Sept. 13, 1948 because of transitory, dull, aching pain in the lower right abdominal quadrant of 1½ years' duration, at which time stool examination revealed ova and parasites which were not positively identified but were thought to be ascaris lumbricoides. The onset of this pain was rather insidious and occurred while he was returning from duty in the South Pacific in 1946. These attacks of pain were unrelated to activity, rest or bowel movement. They were not associated with diarrhea or melana.

The patient returned to his work and remained symptom free until November 1948 when he began to experience intermittent attacks of jerking movements of the right extremities, dizziness and occasional fainting spells accompanied and followed by right frontal headache which was very severe but which would disappear about 1 hour after reclining. These attacks continued intermittently for several months and became so incapacitating that they seriously interfered with his working efficiency.

In February 1949 the attacks of headache and dizziness became more severe although they were no longer accompanied by the jerking movements of the right extremities. The patient consulted an ophthalmologist because in addition he had noted some double vision. No ocular pathology was found. Soon the patient began to notice more frequent bouts of diplopia, usually present with the attacks of dizziness and headache. In March 1949 he had convulsive movements of the right extremities followed by a feeling of right hemianesthesia. Daily vomiting had occurred for approximately 5 days and his frontal headache was much more severe.

His wife stated that for 18 months she had noted considerable personality change, especially marked in the last 6 months, in that he wished to withdraw from

society, was very irritable and depressed, and had predicted his own death.

Examination. On admission Mar. 11, 1949 examination revealed an acutely and critically ill, semicomatose patient with mucous rales in the throat, inability to swallow, dyspnea, cyanosis and profuse perspiration. There was bilateral papilledema of 1 D. One plus stiffness of the neck was noted. There was no tenderness nor rigidity of the abdomen nor were any masses palpable. The patient was completely aphasic and dysphagic and was aroused with some difficulty. There was a right central type facial weakness. The deep reflexes of the extremities were hyperactive, more marked on the left. The plantar response was flexor on the right and equivocal on the left. The Hoffmann sign was positive on the right. The patient was incontinent of urine and feces.

Lumbar puncture yielded a clear, colorless fluid under 140 mm. of water pressure. The cell count, chemistry and colloidal gold curve were normal. WBC was 19,150: 83 per cent neutrophiles, of which 55 per cent were segmented, 14 per cent lymphocytes, 1 per cent myelocytes and 2 per cent eosinophiles. The stool specimen was positive for ova of Schistosoma japonicum.

Course. Tartar emetic therapy was begun. The patient gradually improved and by March 21 could swallow liquids. However, he remained very depressed and cried considerably. He was able to speak several unrelated words. He exhibited left hemiparesis, right central type facial weakness, irregular pupils with the right being larger, bilateral papilledema, bilateral weakness of the 9th and questionable paralysis of the 12th cranial nerve. The left Hoffmann was positive and the plantar response was bilaterally extensor. Deep reflexes of the lower extremities were increased, being more marked on the left. X-rays of the chest and skull were normal. Stool examination on March 21 still revealed ova of Schistosoma japonicum, although all subsequent stool examinations were negative for the ova. Complement fixation test for Schistosoma japonicum was reported as negative. Skin testing was not done as the antigen was not available.

Subsequently it was found that the left side of the tongue was hypesthetic. Hyperesthesia over the 2nd branch of the right 5th cranial nerve was also noted. The patient was still unable to protrude his tongue or to phonate, and no movement of the palate was noted.

Operation. The patient continued to improve generally and on June 15, 1949 ventriculography was done. On entering the parenchyma of the brain through the right occipital burr hole some resistance was encountered and the right ventricle was entered with extreme difficulty. However, air passed freely from one ventricle to the other. The ventriculograms showed asymmetry of the bodies of the lateral ventricles with a slight depression in the roof of the body and occipital horn of the right lateral ventricle and a shift of the ventricular system to the left.

A right parieto-occipital osteoplastic craniotomy was then carried out. On elevation of the bone flap the dura was noted to pulsate normally and gave no evidence of increased intracranial pressure. On reflection of the dura, there was no evidence of the millet seed-like adhesions indicative of surface schistosomiasis, as described.

Exploration was made through the right posterior superior parietal gyrus and an area of resistant grayish, translucent, firm, tough tissue was encountered from which several biopsies were taken. Throughout the whole exposure of the parieto-occipital cortex, the shotty induration could be felt, giving the impression of disseminated granulomatous lesions throughout the subjacent areas of this hemisphere. It was deemed that such a lesion was not removable and therefore further manipulation following biopsy was not carried out.

Pathological Report (Dr. Ferdinand C. Helwig). Granuloma of the brain containing ova of Schistosoma japonicum. The ventricular fluid contains free floating ova of Schistosoma japonicum. (This finding, to our knowledge, has never previously been described in the literature.)

Course. Because of poor postoperative response lumbar puncture was done on June 17, the fluid being under pressure of 320 mm. of water. The laboratory reported that the fluid contained ova of Schistosoma japonicum. Specific tartar emetic therapy was reinstituted and was continued until time of death.

On June 18 the patient exhibited right facial twitchings which occurred during his sleeping hours as well as when he was responsive. At times twitchings would involve the left upper extremity as well. On June 20, left-sided Jacksonian seizures occurred, which were controlled by dilantin and phenobarbital. On June 21, his condition had improved although a left hemiplegia was still present as well as some twitching of the left face, most marked about the mouth. He continued to improve generally until July 1, when his temperature suddenly rose to 104°F. Cyanosis and rales in both lungs developed, and the patient expired on July 4, 1949.

Autopsy. Multiple sections taken from the brain, including the cerebellum and the meninges covering the cerebellum, the basal ganglia, floor of the lateral ventricle, and cerebral cortex, all show a similar lesion. In the areas of softening noticed grossly there is extensive encephalomalacia with loss of substance and large numbers of gitter cells. The capillaries are packed with red blood cells. The adjacent tissue generally shows vacuolization and a very few protoplasmic astrocytes were noted in some instances. Glial cells were frequently noted alongside the blood vessels. In a single one of the many sections taken from the cortex, there was found one multinucleated giant cell similar in structure to those found in the lungs. A very careful search failed to reveal the presence of a single ovum. In some instances, however, dark blue-staining bodies are present, particularly in the meninges covering the cerebellum.

Following failure to identify the ova in any of the sections taken, the sediment from the solution in which the brain was stored was concentrated and examined. By that time the brain was in Kaiserling III, having been successively in formalin and Kaiserling I and II. In the wet preparation, structures resembling the ova of Schistosoma japonicum were found. Sections of cerebral vessels and the choroid plexuses were then macerated and examined. In this wet preparation many oval and round structures were present, some of them resembling Schistosoma japonicum and some of them corpora amylacea. In the stained preparations any distinction was very questionable.

Along with the routine material, the concentrated sediment from Kaiserling III was forwarded to the Army Institute of Pathology for further examination and evaluation.

SUMMARY

A review of the literature on Schistosoma japonicum is presented, with particular reference to ectopic lesions that involve cerebral tissue.

A report is made of 3 cases which came under the authors' personal observation and which were surgically verified. Certain heretofore unreported clinicopathological features of the lesion are described which may be of help in identifying this lesion at the operating table. For the first time also, it is believed, the isolation of the ova of Schistosoma japonicum from the cerebrospinal and ventricular fluid is reported.

Case 3 is of particular interest in that it was verified surgically by both the

biopsied tissue and ventricular fluid removed at the operating table but could not be verified at autopsy in a patient who had been under intensive antimony tartrate treatment following surgery.

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IS THERE ROOM FOR A NEUROLOGIST IN A NEUROSURGICAL WORLD?*

JOSEPH C. YASKIN, M.D.
Department of Neurology, Graduate School of Medicine, University of Pennsylvania, Philadelphia

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How are the mighty fallen!
Tell it not in Gath,
Publish it not in the streets of Ashkelon;
Lest the daughters of the Philistines rejoice.

This quotation from Chapter 1, II. Samuel, portrays my feeling as I address this Society. I must admit that the feeling is not one of marked anxiety or depression, but just one of general apprehension mixed with a bit of hope that by "catharsis" I may be able to improve my own situation and perhaps influence the neurosurgical mind to be at least more kindly inclined toward the downtrodden neurologist.

To appreciate the present place of neurology in the world of neurosurgery, it is necessary briefly to allude to the evolution of neurology, its relation to other branches of medicine, and to evaluate the several factors that may play a part in determining the present role of neurology in the world of neurosurgery.

Neurology was at all times only a small branch of medicine. It was never a large empire. In keeping with the above-mentioned quotation from the Bible, it always remained a small country at the junction of Africa and Asia, and has always been threatened by the great powers from the north, east and west; whether they were Persians, Greeks, Romans or later the Turks. Like the little country in north Africa, it nevertheless was able to preserve some semblance of a soul of its own. In ancient medical history, neurology shared the superstitions and the objective knowledge of its times. It would appear that it was the physician rather than the then unknown surgeon who did the trephining of the skulls in ancient Egypt. In the period prior to Galen, little concrete was known about anatomy, the function and the disorders of the nervous system. Relatively little was learned during the so-called Dark Ages. The Renaissance contributed considerably to the anatomy and began to contribute toward the localization. However, it was not until the latter part of the 18th century, and especially during the 19th and present century, that strides were made by individuals who were interested in the various parts of the nervous system. Although anatomists and physiologists have achieved a great deal, it was the clinical neurologists, who were often also the neuropathologists, who clarified the intricacies of many of the diseases

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now amenable to treatment by surgery and other means. It should be born in mind that until the turn of the century there were no chairs in neurology even in the great medical schools of the world, and that even now there are some schools where neurology is considered a sub-specialty in internal medicine, which I believe it should be.

Unfortunately, until recent decades, neurology remained largely a descriptive, though interesting branch of medicine. There was much preoccupation with anatomical, pathological and physiological factors, and all too little therapy. It was the neurologist who elucidated the nature of diseases that are now attacked by chemotherapy, substitution therapy and surgery. The neurologist prepared the soil to be taken over by the internist, pediatrician and the so-called syphilologist, and by the surgeon. The neurologist, on the surface, appears to have outlived his usefulness. Pernicious anemia and other deficiency states are generally taken over by the well trained internist. All forms of syphilis belong to the dermatologist. The neurosurgeon, who ordinarily has little time for detailed histories or neurological examinations, short-cuts his diagnoses by contrast medium studies and is often impatient about the academic attitude of the neurologist. At best the general surgeon and the neurosurgeon are a trifle impatient with individuals who do not wield the scalpel, the hemostat and the bovie. The motor expression in their work sometimes fails to neutralize their inborn and developed drives, which are at times erroneously designated as aggression.

The woes of the neurologist have, in the past 50 years, been further increased by changes in psychiatry. At the turn of the century most of the neurologists were interested in and practiced psychiatry. They believed that disturbances in feeling, thinking and acting in the great majority of cases should be closely related to the cerebrospinal and vegetative nervous systems. At the turn of the century, modern psychopathology and psychotherapy had rapidly assumed great importance and reached a plateau where there are those who believe that one need not know any medicine to be a psychopathologist or psychotherapist. In the last few decades men have been trained in both neurology and psychiatry, but either because of intrinsic interest in psychiatric problems, and perhaps for monetary considerations, or both, these individuals in many communities drop their neurology and devote themselves to psychiatry, leaving the community and often hospitals without any one trained in organic neurology. The neurosurgeons, on the other hand, feeling their "oats," get fairly good training in neurology and often unwittingly become the neurological consultants in small and even in good-sized communities.

It is true that there is a definite change in neurological thinking, at least among the younger neurologists who survive these various invasions into neurology. There is a tendency on their part to return to the earlier concepts that neurology is a part of internal medicine, clinical and experimental, and they devote their energies along these directions, finding a place for themselves, at least in the larger medical centers of the world. They attempt to

investigate conditions that are not as yet understood from the standpoint of etiology, pathogenesis or pathophysiology and are not amenable to various forms of therapy, including neurosurgery. There are plenty of unchartered continents in medicine, and especially in neurology and psychiatry. Those of us whose blood vessels are becoming sclerosed still believe that a great many of the major psychoses have structural or chemical bases to account for both their physiological and psychological disturbances. The various forms of brain surgery and shock therapy are to my mind merely stepping stones to a better understanding of these diseases.

The neurologist is still of some help to the busy internist or to the internist who is broad enough to know that he cannot be well informed on the many sub-specialties of internal medicine. Does he have a place side by side, or at least at the periphery of the world of neurosurgery? This depends on several factors, both communal and individual.

In a small community, where there are no trained neurologists or where the neurologists turn to shock therapy and psychotherapy, the neurosurgeon automatically becomes a neurological consultant. It is he who is undoubtedly called upon to see strokes, motor weakness and the various painful conditions. He often treats, with or without the aid of the internist, conditions that are definitely not neurosurgical and are definitely neurological. This happens often with busy neurosurgeons, to say nothing about the young man who has some time on his hands, and is glad to have this additional practice.

In larger communities, and especially in those that have teaching institutions, the situation is and at times could be different. On the one hand, the well trained neurologist has referred to him many cases which in other communities would go directly to the neurosurgeon, or he may be fortunate enough to be associated with a kindly understanding gentlemanly neurosurgeon, who prefers the preliminary work to be done in the department of neurology. This venerable type, like the old-time doctor with a frock coat and striped trousers, is largely disappearing. Frequently the neurologist in a good many clinics gets a reference from the neurosurgical department after air studies, arteriograms, myelograms and other contrast medium studies, and surgical therapeutic tests have failed. The patient is then referred, not reluctantly or with a feeling of defeat, but occasionally with disdain, to the academic person known as the neurologist for further study and perhaps psychotherapy. One wonders whether the past generation, as portrayed by the relationships of Spiller and Frazier, is not better than the arrangement existing in a good many clinics at the present time.

What, then, can the neurologist do in the present-day neurosurgical world, such as it is? Those who wish to survive in this specialty must, like certain historical entities, find new means of serving, being tolerated, and, when possible, making themselves more or less indispensable in this changing world. They must remain good internists. If they have the capacity and means they should pursue some form of investigative work that may aid

diagnosis, but especially therapy. Above all, they must remain bedside clinicians, which implies the obtaining of careful histories, good physical examinations, neurological and somatic, and the ability to select and evaluate laboratory procedures, and they must develop and, above all, maintain an accurate evaluation of a given patient, physically and psychologically. They will find a place for themselves in the *early detection* of the several conditions that are amenable to medical treatment and the early detection of conditions that are amenable to surgical treatment. They may even serve the neurosurgeons in steering them from operating in wrong places, and from operating on conditions that are not surgical to begin with. They may help him to avoid doing the kind of surgery that brings further discomfort to the patient and discredit to the specialty. I may venture to say that in some clinics the neurosurgeon needs a deterrent from doing a lot of things he would not do if proper consideration were given to the subject.

SUMMARY AND CONCLUSIONS

Neurology has at all times been only a part of internal medicine. It helped in the course of years to clarify the understanding of diseases of the nervous system and prepared the background for the various forms of therapy, including neurosurgery. In keeping with the evolution and various aspects of the medical sciences, it has outlived much of the usefulness that existed up to a few decades ago. It has to turn to new fields of activity to remain a dynamic factor in medicine. It is still felt that neurology as an entity has a definite place in internal medicine and even in neurosurgery.

CASE REPORTS

CHRONIC SUBDURAL HEMATOMA IN AN ADULT PRODUCING MARKED EROSION AND PERFORATION OF THE OVERLYING DURA AND SKULL

REPORT OF CASE WITH OPERATION AND RECOVERY*

J. M. MEREDITH, M.D., AND GEORGE R. GISH, JR., M.D.†
Department of Neurological Surgery, Medical College of Virginia, Richmond, Virginia

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Recently we have observed in our clinic a colored man aged 32 years who was admitted to the hospital with the chief complaints of occipital headache and pain in each eye. Drowsiness had developed only in the previous 24 hours, and there had been extreme weakness of each leg (suggesting a cord tumor) the last few days before admission. The patient eventually was proved to have three chronic subdural hematomas—two separate (frontal and parietal) clots on the left side, and a single frontal subdural clot on the right side. The two frontal clots were connected beneath the falx as shown by irrigation at the time of operation. What makes this case of more than usual interest, however, is the fact that there was *marked erosion* and even *gross perforation* of both tables of the skull in the left parietal region, easily visible roentgenographically, overlying the largest of the three chronic subdural hematomas. It is this pathological rarity that has primarily prompted the present report.

CASE REPORT

M. C. V. Case #110273. P.W., a 32-year-old colored male dry-cleaner, was admitted to St. Philip Hospital on March 8, 1951. He was referred by Dr. Robert Turner of Gloucester, Virginia, who stated that the patient had become ill in a distant city 2 weeks previously. His chief complaint had been "weakness of my legs." He also complained of occipital headache and pain in each eye. The day before admission he had become quite drowsy. There was no history of trauma.

Past history was irrelevant except for three fractures of the right femur as a boy.

Neurological Examination. The right pupil was larger than the left and reacted to light less briskly. There was questionable slight primary atrophy of the optic disks bilaterally. The tendon reflexes were brisk and equal on each side and no pathological reflexes were elicited. No other definite localizing signs were demonstrated that might suggest a surgically significant cerebral or cerebellar lesion. A diagnosis of a spinal cord lesion (? tumor) producing weakness of the legs was also considered.

Laboratory Studies. Spinal puncture on the day of admission disclosed an initial pressure of 300 mm. water (? complete relaxation of the patient). Five days later another spinal puncture was performed and an initial pressure of 240 mm. water was demonstrated. The fluid was grossly quite clear; 4 cc. were removed, the final pressure being 170 mm. water. A Queckenstedt test (to rule out a surgically significant cord lesion as the cause of the bilateral leg weakness) showed a rapid rise and slower fall of fluid in the manometer, the patient not being

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† Former Resident Neurosurgeon, Medical College of Virginia, Richmond. Present address: Emory University Hospital, Emory University, Georgia.

entirely relaxed or cooperative. The CSF contained 40 mg. per cent total protein, and 3 lymphocytes per HPF; Wassermann reaction was negative. The blood flocculation test for syphilis was negative. The fasting blood sugar was 104 mg. per cent and the NPN 33 mg. per cent. Urinalysis was negative. RBC 4.86 million per HPF; Hb. 13.5 gm. per cent; WBC 5,200 per HPF, with 67 polymorphonuclears, 28 lymphocytes, 3 mononuclears and 2 eosinophiles. An EKG on March 9 showed sinus tachycardia.

Roentgenograms of the skull showed a large (4×6 cm.) area of bone destruction and (over a smaller area) *complete erosion* of both inner and outer tables in the left parietal region (Figs. 1 and 2). This rarefied and perforated portion of bone was not associated with or surrounded by any area of bony thickening, trabeculation or vascularization to suggest that it might be an osteolytic bone tumor, an angioma of bone or other primary osseous tumor or disease of

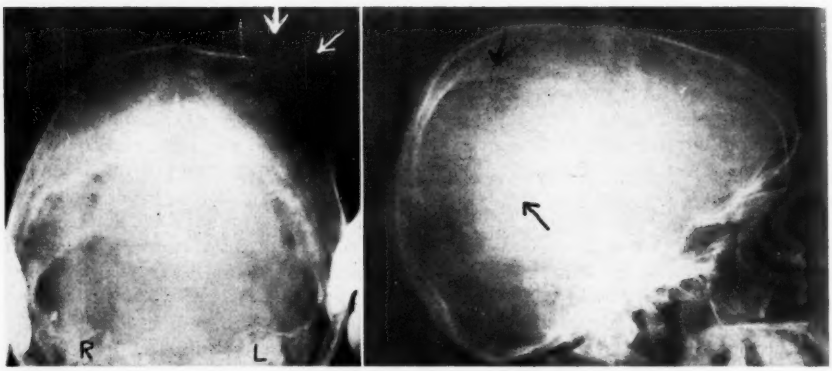

FIG. 1. (*Left*) Anteroposterior roentgenogram showing (arrows) the erosion and actual perforation (at least 1 cm. in diameter) of the skull in the left parietal area directly overlying the largest of the three chronic subdural hematomas in this patient.

FIG. 2. (*Right*) Left lateral view.

the skull or underlying structures. One gained the impression, rather, that it was an erosion of otherwise normal bone by an underlying soft-tissue expanding lesion, the nature of which (chronic subdural hematoma) was entirely unsuspected by any member of the neurosurgical staff before operation, there being no history of specific trauma in this case. One could not, however, from the X-ray appearance of the skull alone, entirely exclude the diagnosis of a primary bony tumor.

Left carotid arteriography done on March 12, 1951 gave normal findings; no undue vascularity of the cerebral, skull or scalp tissues on the left side was disclosed.

1st Operation (G.R.G.). On March 15, 1951, bilateral frontal burr openings were made for ventriculography; these revealed a moderate-sized bilateral frontal subdural hematoma of the chronic variety; ventriculography was therefore abandoned. Irrigation of one subdural space was followed by the appearance of the fluid in the opposite subdural space very promptly, as though it went under the falx. The cerebral (frontal) cortex was 2.0 cm. or more beneath the dura bilaterally after the clots had been evacuated.

Separate analysis of the two fluids was carried out in the laboratory. That from the right frontal subdural space contained 1.8 gm. Hb., 280,000 RBC per HPF and 700 WBC, 60 per cent of which were lymphocytes and 40 per cent polymorphonuclears. The fluid from the left subdural space yielded similar results, i.e., 2.0 gm. Hb., 295,000 RBC per HPF and 800 WBC, with 54 per cent lymphocytes and 46 per cent polymorphonuclears.

Microscopic Examination. A small portion of the subdural membrane from each side was examined. It was composed of fibrous and collagenous tissue with infiltration of lymphocytes,

plasma cells and eosinophiles. Small areas of recent hemorrhage were noted. Diagnosis: subdural membrane—bilateral—following subdural hematoma.

Course. The patient was hydrated with 3,000 cc. of fluids per day intravenously or by hypoclysis in an effort to bring about early expansion of the bilaterally compressed cerebral hemispheres. There was marked clearing of his stuporous state, and he was able to be out of bed on the 3rd postoperative day.

Although the finding of a bilateral chronic subdural hematoma through frontal burr openings was most interesting and resulted in great improvement in the clinical status of the patient, the erosion and apparent perforation of the left parietal region of the skull (noted on the roentgenograms and also easily palpable as the lesion was quite painless) were still unexplained. Accordingly, a second operative procedure was undertaken.

2nd Operation (G.R.G.). On March 29, 1951, under endotracheal gas-ether anesthesia, a horseshoe-shaped scalp flap was turned down over the bony defect. There were three small areas (each about 1 cm. in diameter) in the skull, which appeared to have been completely or almost completely eroded by underlying pressure. One could see a purplish mass beneath the cranial defects. A bone flap with four burr holes was made encircling the three perforated areas of the skull, and turned down and sacrificed without incident, leaving an exposed area of dura 6×4 cm. in diameter. There was no extradural neoplastic or granulomatous tissue seen. The dura was likewise perforated by the underlying mass which, through the otherwise intact dura, felt fluctuant, even resembling a vascular tumor. However, when the dura was opened, the hinge being near the midline, the typical outer membrane of a chronic subdural hematoma was found—greenish-purple in color. This outer membrane was excised around the dural margin after removal of the clot, which was practically of liquid type without appreciable solid elements. The inner membrane was rather readily excised by stripping it off the underlying cerebral cortex. This hematoma did not appear to be a direct extension or a part of the left frontal subdural clot removed at the first operation 2 weeks previously. At the time of dural closure, the cerebral cortex began to expand normally and looked rather healthy. There was nothing in the area of exposed cortex to suggest that the subdural clot had originated as bleeding from a tumor or other pathological lesion of the cortex or subcortical area. A tantalum plate was inserted over the resutured dura, being held in place with three tantalum screws. The scalp was closed with layers of interrupted silk sutures.

Pathological Studies. Gross examination. The removed bone flap measured 8 cm. in its maximum diameter. Its greatest thickness was 0.7 cm. In the central portion of the bone was an opening, 1 cm. in diameter, which penetrated through the entire thickness of the specimen. The outer surface of the bone flap was convex, smooth and pale yellow in color. The inner surface was concave and characterized by multiple areas of depression. Some of these were shallow; others, however, were quite deep and penetrated almost through the entire thickness of the bone so that light could easily be seen through them. The deepest of these had bases that were translucent.

Microscopic examination. Through an oversight, the microscopic study of the decalcified bone specimen was apparently never carried out. The membranes removed at this operation were typical of those seen in chronic subdural hematoma. Diagnosis: chronic subdural hematoma with erosion and perforation of overlying dura and calvarium (left parietal).

Course. The patient made an uneventful recovery and was ambulatory 48 hours after operation. On neurologic examination 8 days postoperatively he was alert and cooperative. The optic disks were well outlined. He moved all his extremities very well. There was no inequality of reflexes and no positive Babinski sign or ankle clonus on either side was present. Sensation was normal in all extremities. He had no headache or vertigo. He was discharged April 9, 1951, 11 days after operation, much improved. Repeated questioning of the patient had elicited no history of trauma.

Subsequent Reports. April 25, 1951, 27 days after 2nd operation. The patient had no complaints although there was found very slight muscular weakness of the left arm and leg. There had been only one headache since hospital discharge, with spontaneous relief. His speech was a little slow but he was not definitely aphasic. He was anxious to return to his usual work in

a distant city. He was advised, however, to rest several months more because of the severity and multiplicity of the lesions to which he had been subjected.

Sept. 9, 1951, slightly more than 5 months after 2nd operation. The patient replied to our letter of inquiry, writing an exceptionally legible hand: "I received your nice letter; was glad to hear from you. I am getting on nicely. I don't have any trouble with my head. Thank you again for being so interested in me. I am planning to return to work this week." Apparently his condition was excellent and he had no subjective complaints of any kind; the family physician corroborated this statement by letter.

April 2, 1952, slightly over 1 year after operation. A letter from his physician stated that the patient was in excellent condition, without complaints of any kind, and that he was working daily in a tailor shop.

DISCUSSION

Several volumes on neurology and on neurosurgery[1,3,6,9,12,14,16,19] and many articles [5,7,8,10,11,15,17,18] having to do with chronic subdural hematoma and head injury in general have been examined recently by the writers, but no description of a lesion similar to that in our own case was found. There was no evidence of neoplasm of any kind associated with the bilateral subdural hematomas, three of which were disclosed in two operations, and over only one of which (left parietal) was the calvarium eroded and perforated.

Although it is unfortunate that the bone flap with the perforation was not examined microscopically, it is unlikely that it contained any pathological process except erosion and perforation of the skull since the pre-operative carotid angiogram showed no unusual vascular pattern, and also because of the operative findings and the continued well-being of the patient over a year after the operation.

Dr. F. B. Mandeville,[13] Director of the Medical College of Virginia Roentgenology Department, and Dr. Vincent W. Archer,[2] Director of the University of Virginia Roentgenology Department, know of no similar verified case in their combined experience. The fact that there was no history of trauma in this case is not too disturbing to us as the patient had a low I.Q., and one could not entirely exclude a history of alcoholism—such patients being notoriously prone to subdural hematomas.

It is not unusual to find greatly thinned calvaria, simulating congenital hydrocephalus, in young infants with chronic subdural hematoma. One may even see a very asymmetric skull protruding locally over a subdural clot, as in a 24-month-old white male child operated upon by our colleague Dr. C. E. Troland (March 1952). This patient had a very prominent asymmetrically protruding left parietal calvarium, beneath which was an enormous chronic subdural hematoma, following the removal of which complete and early recovery from stupor and other disabling symptoms ensued. Similarly, Dr. Arthur Childe of Winnipeg, Canada, at a meeting of the American Roentgen Ray Society in September 1951, described 8 cases of chronic subdural hematoma or hygroma with localized enlargement and thinning of the cranium over the subdural fluid collection, but none of his patients[4] had an actual skull defect or perforation of the calvarium, as did our adult patient. The present case, therefore, is believed by us to be in a unique pathological category.

SUMMARY

The case of a 32-year-old colored male is presented who had three chronic subdural hematomas; two were over the left cerebral hemisphere and one was over the right cerebral hemisphere. There was no history of trauma. However, even more

unusual than these findings, was the demonstration of marked erosion, destruction and actual perforation of the skull overlying the left parietal hematoma. This area of bony erosion and perforation was removed and a tantalum plate was substituted. The three subdural hematomas and the involved bone were all removed in a two-stage procedure, with early complete recovery of the patient and his return to his usual employment in slightly more than 5 months after the second operation. In a little over a year after operation, he continued in excellent condition. The case is unique in our experience, and the pathological explanation of the bony destruction and perforation of the skull over the clot is obscure.

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DISSEMINATED OLIGODENDROGLIOMA

William V. Trowbridge, M.D., and John D. French, M.D.

Neurosurgical Section, Surgical Service, Veterans Administration Hospital, Long Beach, California

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The oligodendroglioma is generally considered to be a tumor of relatively benign type.[13,18,25] It is on the basis of accumulated survival statistics that such a classification is derived; and in this sense, the statement is true, for patients with oligodendroglioma ordinarily survive for longer periods than do those with some of the other types of gliomata. Nevertheless, it was suggested by Eisenhardt in 1935[9] that

possibly these tumors are not as benign as they were once thought to be. Numerous reports since that time have tended to substantiate this latter view. Indeed, Kernohan[16] has said of the subtype, the oligodendroblastoma: " . . . at times, these are the most malignant tumors affecting the central nervous system." The limitation of malignant potentialities to the oligodendroblastoma group was later tacitly denied by Earnest, Kernohan and Craig[8] in their assertion that a division of these tumors into oligodendrocytomas and oligodendroblastomas could in no way be related to survival time.

Specific evidence of the malignant potentialities of this neoplasm has been found in the reports of Löwenberg and Waggoner[20] and Bailey and Bucy[3]. In the cases reported by these authors there appeared to be a tendency of the tumor to invade the leptomeninges, pachymeninges, and even the scalp. More virulent malignancy was reported by James and Pagel[14] in whose case there was widespread metastasis of an oligodendroglioma to mesodermal tissue. The invasion of mesodermal tissue by such a tumor had previously been reported by Kernohan, Woltman and Adson[17] in a case where the primary lesion arose from the cauda equina.

Since the extent of metastasis is held to be approximately proportional to the malignancy of the primary tumor,[5] it is notable that isolated reports of subarachnoid metastasis from oligodendroglioma are to be found. In 1945, Blumenfeld and Gardner[4] published an excellent review of 11 such case reports, and added 1 case of their own. It was briefly mentioned by Earnest and his co-workers[8] that subarachnoid seeding was present in 14 of their 165 verified cases of oligodendroglioma.

The present report is prompted by the divergent opinions concerning the malignancy of these tumors, and the infrequency of their reported dissemination through the subarachnoid space.

CASE REPORT

G. H., a 38-year-old white male, began to suffer from generalized convulsions in 1943. These were controlled with standard anticonvulsants until 1945, when a craniotomy revealed a right temporoparietal oligodendroglioma. From that time, there was progressive development of multiple neurologic deficits, and another craniotomy was performed in 1949 in an attempt to again radically remove the tumor. The development of severe weakness in the left limbs, together with constantly increasing headache, led to the final admission in November 1950.

Examination. The patient appeared to be somnolent. He was rational, although cerebration was attenuated. There was considerable elevation of the right temporoparietal bone flap. He had a very severe left hemiplegia, and hypesthesia and hypalgesia were present over the entire left side of the body. Left homonymous hemianopia and a left facial palsy of central distribution were also present. There was no papilledema.

Hospital Course. Cerebral angiography was performed revealing a pronounced anterior displacement of the middle cerebral vessel group on the left. Approximately 3 weeks after admission, the left temporoparietal bone flap was again turned down, and another large portion of the tumor was removed. Although subjective improvement immediately followed this operation, the patient's condition continued to deteriorate, and he expired in April 1951.

Gross Examination of the Brain. The right temporal and occipital lobes appeared to be totally replaced by tumor. Inspection of the brain stem revealed grayish, granular material covering the pons and medulla, and this had the appearance of tumor seedings. The dura over the right occipital lobe was quite adherent to the tumor mass, as was the tentorium on the right. Coronal section through the region of the optic chiasm revealed the tumor mass to be almost completely replacing the hypothalamus. The right lateral ventricle was distended and its walls were lined with small, gray, granular nodules. What appeared to be tumorous tissue was found to be compressing the brain stem in the region of the corpora quadrigemina,

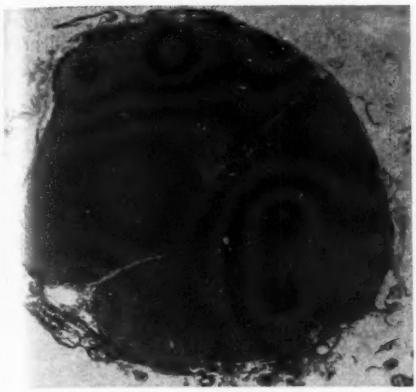

FIG. 1. Section at the level of pyramidal decussation showing tumor implant in the caudal appendage of the 4th ventricle. Hematoxylin and eosin, ×4.

FIG. 2. Section at the level of the inferior olivary nucleus demonstrating the metastatic tumor nodules on the floor of the 4th ventricle. Hematoxylin and eosin, ×3.

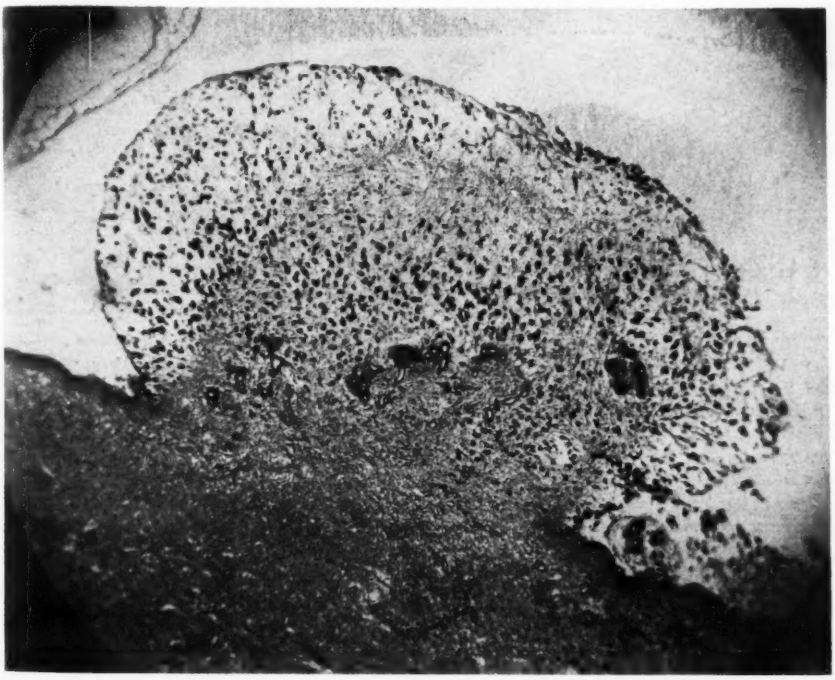

FIG. 3. Low power detail of tumor implant on floor of the 4th ventricle. Hematoxylin and eosin, ×55.

and the interpeduncular space was entirely filled with this type of tissue. A section through the cerebellum and brain stem revealed severe dilatation of the 4th ventricle, the walls of which were also found to be studded with small, gray, granular nodules.

Microscopic Findings. Hematoxylin and eosin preparations were made of both the main tumor mass and the small ventricular nodules. A large tumor implant was found in the terminal appendage of the 4th ventricle (Fig. 1) at the point where it became the central canal. Sections through the brain stem revealed similar tumor implants in the 4th ventricle (Figs. 2 and 3) and the leptomeninges.

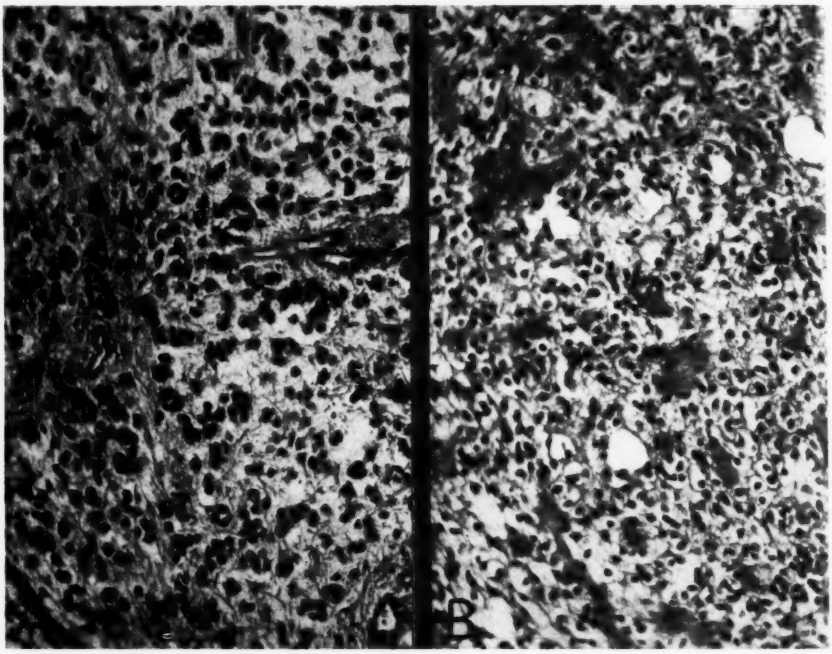

FIG. 4. (A) Cellular detail of tumor implant as found at autopsy. (B) Cellular detail of surgical specimen from primary tumor mass obtained 16 months prior to death. Hematoxylin and eosin, ×200.

The cellular structure, both in the main tumor mass and in the implants, was that of an oligodendroglioma (Fig. 4A). These sections were very similar to those obtained previously at surgery (Fig. 4B), although there was evidence of increased malignancy as shown by the greater variation in nuclear size and the presence of increased hyperchromatism of the nuclei. Cords of tumor cells were present, separated by great spaces which contained only a delicate fibrillary material. The tumor cells themselves were rather uniform, with round to bean-shaped nuclei (Fig. 4A). Usually there was very scanty cytoplasm and no visible nucleolus. Occasionally, atypical tumor cells were present which showed 2–3 fine nucleoli and no other nuclear structure. The tumor cells were collected in clumps and nests of varying size. Evidence of mucinous degeneration was seen in all sections studied.

DISCUSSION

Although gliomas tend to spread primarily by direct extension,[5] it has long been known that they may disseminate through multiple implants in the subarachnoid

space.[3,10,11,22–24] Spread of this nature is most commonly seen with the medulloblastoma,[10] although it has been reported in association with the ependymomas,[5,23,24] glioblastomas,[5,10,23] astrocytomas[5] and choroid plexus papillomas.[12,25] In spite of the general recognition of this type of neoplastic spread, many of the standard textbooks of neuropathology show a conspicuous absence of reference to this phenomenon in association with the oligodendroglioma.[1,2,7,15,19,26]

The mechanism responsible for such dissemination appears to be a simple exfoliation of viable tumor cells into the cerebrospinal fluid, in which medium these cells are distributed to all parts of the subarachnoid space. It would seem that the cellular exfoliation could spontaneously occur from the surface of a neoplasm, although it has been suggested[12] that the disengagement of tumor cells is probably due to trauma. The observation that these tumors frequently become more malignant following surgical attack[2,24] hardly holds true in this case where the patient survived for 5 years following his first craniotomy. It has been shown by Chusid[6] that, in the ependymomas at least, subarachnoid seeding is often well established at the time of the initial operation.

Since the oligodendroglioma constitutes only a small percentage of the gliomas[2,15,20,21] the accumulation of isolated reports of subarachnoid metastasis gains considerable significance. These data tend to support the thesis of Blumenfeld and Gardner[4] offered in their statement that this glioma is second only to the medulloblastoma in its propensity to seed through the subarachnoid space.

The implications associated with such a tendency are obvious from a therapeutic standpoint. Since this manifestation of the neoplasia seems to appear late in its course, attempts at radical excision of the tumor growth at the earliest possible moment would seem to be imperative.

SUMMARY

1. A case is reported in which there was extensive subarachnoid metastasis from a cerebral oligodendroglioma.

2. In view of the accumulating data regarding the tendency of these gliomas to invade and metastasize, a revision of the existing opinions concerning their "benign nature" would appear to be indicated.

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PARAPLEGIA FROM RUPTURED LUMBAR DISCS IN ACHONDROPLASTIC DWARFS

Frederic Schreiber, M.D., and Herbert Rosenthal, M.D.
Division of Neurosurgery, Harper Hospital, Detroit, Michigan

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A herniated nucleus pulposus can be especially serious in the achondroplastic dwarf because of his abnormally narrow spinal canal. Two such dwarfs were operated on by us during the past year with relief of pain and paralysis caused by a ruptured nucleus pulposus between the 2nd and 3rd lumbar vertebrae. Although a number of cases of achondroplastic dwarfs with paralysis of the lower extremities are recorded in the literature, we could find no previous report of a ruptured disc being the cause of paralysis in these cases.

In appearance the achondroplastic dwarf differs from the normal because of the marked shortening of his extremities and the unusual shape of his large head. In utero there are some disturbances of cartilaginous centers[1] especially of the epiphyses of the long bones, causing a retardation in long-bone growth later in life. By x-ray examination at birth, the spinal column of the achondroplastic is normal in length and curvature. However, the entire spinal canal is narrower than normal because of the shortness of the pedicles. As these dwarfs continue to subject their spinal column to the stresses and strains of everyday life, many will show changes in spinal curvature.

Fairbank[3] pointed out that in achondroplastic dwarfs the spines are extremely lordotic, but often the dorsolumbar spines are surprisingly flat. Sometimes the apparent lordosis results from the unusual prominence of the buttock.

Donath and Vogl[2] described more or less marked changes in the physiologic lordosis of these dwarfs at the dorsolumbar region. From the 12th dorsal to the 3rd lumbar segments the vertebral bodies show a definite wedging of varying degree. Thus the achondroplastic dwarf has an inherent weakness of the spinal column manifested by dorsolumbar kyphosis. Whereas some show flat backs, others reveal distinct gibbous formation at that level.

There are earlier cases in the literature of achondroplastic dwarfs with neurologic symptoms and signs suggestive of cord compression. However, Albrecht and Ranzi,[1] in 1926, reported a case of compressive myelitis upon which they performed a laminectomy. Not only was the diagnosis confirmed but the achondroplastic dwarf retained many lost functions. Donath and Vogl[2] felt that, in their case, arthritic changes above the level of the gibbus caused the formation of osteophytic spurs which encroached upon the spinal cord. Freund,[4] then Kennedy *et al.*,[5] subsequently demonstrated similar findings in case studies. Vogl and Osborne,[7] in 1949, reported another example and developed further the pathogenesis of varying degrees of transverse myelitis in achondroplastic dwarfs as being caused by exostoses encroaching upon a constricted spinal canal. They showed that the entire spinal canal is narrower than a normal adult canal. Since the achondroplastic dwarf's spinal cord is of normal diameter, the cord just fits into the canal with no room to spare. Hypertrophic arthritic changes appear adjacent to and above the gibbous deformity because of the increased motion compensating for the lack of motion at the level of the gibbus.

REPORT OF CASES

Case 1. W. B., a 33-year-old white male auto worker, was well until mid December of 1950 when he noticed pain in both hips and his "feet gave way" while lifting materials and suddenly turning his body. He was taken to a hospital where he was put on bed rest. His hip pain diminished at rest but became very severe with radiation down both legs when he was on his feet. He also noticed numbness, tingling and weakness of his legs. He was admitted to Harper Hospital Jan. 8, 1951, on the orthopedic service.

Examination. The patient was an achondroplastic dwarf. He was in no acute distress. Positive findings were: an absent left knee jerk, an absent right ankle jerk and hypalgesia of the right little toe and lateral aspect of the right thigh. Both legs were weak.

Course. Because he was thought to have a mechanically unstable back, his spine was manipulated under sodium pentothal and a plaster body cast was applied. The patient did well until he was on his feet and then his pain and paresis recurred. He was referred to the neurosurgical service.

A lumbar puncture was done on Jan. 23, 1951, with injection of pantopaque. A few drops of yellowish CSF were obtained; total protein was 3536 mg. per cent. The myelograms revealed a complete block at the level of the intervertebral disc between L2 and L3. The pantopaque did not flow up or down with the patient on the tilt table. This was thought to be consistent with an arachnoiditis.

Operation. A laminectomy was done with removal of the lower four lumbar spines and laminae. The spinal canal throughout was much shal-

FIG. 1. *Case 1.* Achondroplastic dwarf with recovery from pain and partial paralysis in the legs following removal of a herniated lumbar nucleus pulposus.

lower than normal. The dura was blue and nonpulsating. Upon opening the dura, the caud equina was found to be inflamed and tightly squeezed in the dural sac. A large resilient pr trusion between the 2nd and 3rd lumbar vertebrae was palpated beneath the posterior liga ment compressing the caudal roots. These were separated and an incision was made in th posterior ligament at the site of greatest swelling. Numerous fragments of nucleus tissu extruded themselves and were removed with a pituitary rongeur. The dura was not close because of the swollen roots and arachnoiditis. No fusion was done.

Course. The patient had an uneventful convalescence with complete relief of pain (Fig. 1) and was discharged from the hospital on Feb. 19, 1951, wearing a back brace. He returned to his former work after 6 months and had no complaints when last seen 1 year after surgery. He had regained strength in his legs and was free of numbness. His deep reflexes were equal and physiological bilaterally.

Case 2. W. A., a 31-year-old colored female, was asymptomatic until October 1951, when she had vague bilateral hip pain radiating down both legs, especially the right. This was accompanied by numbness of her legs. She was 7 months pregnant at this time and was not too concerned with these symptoms. After she was delivered by cesarean section in mid December 1951, the pain and numbness persisted. On Jan. 19, 1952, she lost bladder sensation and was unable to void. When she tried to walk, her right leg was paralyzed and she experienced tingling sensations in her back and traveling down her lower extremities. She was admitted to the neurosurgical service on the same day.

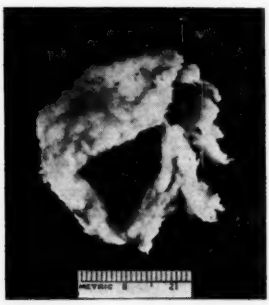

FIG. 2. *Case 2.* Single piece of nucleus pulposus tissue which had extruded itself and was causing pain and paralysis in the legs of an achondroplastic dwarf.

Examination. The patient was a thin achondroplastic dwarf in acute distress. Positive findings were: limited straight leg raising on the right, saddle anesthesia, anesthesia of the lateral aspect of the right foot, absent right knee and ankle jerks and absent left ankle jerk. She was unable to stand or walk.

On Jan. 23, 1952, lumbar puncture and myelography were done. CSF pressure was low. The fluid was xanthochromic; total protein was 2550 mg. per cent. Myelograms revealed a complete block at the junction of the 2nd and 3rd lumbar vertebrae.

Operation. On Jan. 25, 1952, an exploratory laminectomy at L2 and L3 was performed. Spines and laminae were removed, exposing a spinal canal which was narrower than normal. The dura was opened revealing a markedly congested cauda equina, the matted roots being tightly squeezed together. At the level between L2 and L3 on the right a large single herniated piece of nucleus pulposus material could be seen within the dura itself, pushing the conus and cauda from posteriorly (Fig. 2). The piece of nucleus pulposus had ruptured through the posterior ligament and dura and was found lying partially in the canal and partially in the intervertebral space. It was extracted in one piece, which measured $1\frac{1}{2}$ inches in diameter and $\frac{1}{2}$ inch in thickness. Two smaller pieces were removed, and then a catheter was passed up and down the canal without resistance. The dura was left open and the incision closed. No spinal fusion was performed.

The pathological report was "nucleus pulposus."

Course. The patient gradually regained strength in her legs, to the point where she got along well on crutches at time of discharge, Feb. 17, 1952. Her bladder sensation and function returned 1 week after operation.

She was seen 1 month after discharge. At that time her knees were wobbly but getting stronger, as were her legs. She continued to have good bladder function. However, there was still some numbness of the right foot and right saddle area. Two months after surgery she was walking without crutches and the numbness was subsiding.

COMMENT

Both of our patients displayed signs and symptoms referable to a partial compression of the caudal roots. This was confirmed during laminectomy when herniated pieces of nucleus pulposus tissue were found between the L2 and L3 level impinging upon and causing congestion, edema and adhesions of the cauda equina. In the male the history suggests that his lifting and sudden turning were the factors precipitating the ruptured disc. In the case of the female, the strain of her pregnancy probably threw a greater burden on her spine with resulting rupture of her lumbar disc. After laminectomy and removal of the herniated pieces of nucleus pulposus material both dwarfs regained most of their lost motor and sensory functions and became symptom free.

In contrast to our findings of ruptured nucleus pulposus there are reported cases of compressive myelitis at higher levels (D10 or D11), caused by hypertrophic osteophytes. We found no osteophytes but did confirm previously reported findings of a narrowed spinal canal in these patients.

In both of our cases, the spinal column was normal in curvature by x-ray. Many of the previously reported cases revealed exaggerated lumbar lordosis of varying degree resulting from gibbous formation at the dorsolumbar area. This inherent spinal column weakness with wedging of the dorsolumbar vertebrae in some achondroplastic dwarfs may manifest itself in others by eventually herniating a nucleus pulposus under undue stress and strain.

SUMMARY

1. We have reported 2 very similar cases of achondroplastic dwarfs with partial paralysis of the legs and pain caused by a ruptured lumbar interverebral disc. After laminectomy and removal of the herniated nucleus pulposus both dwarfs regained lost motor and sensory function.

2. In reviewing the literature there were found reported cases of achondroplastic dwarfs with varying degrees of compressive myelitis resulting from impingement of exostoses on the spinal canal.

3. Whereas some achondroplastic dwarfs form gibbi because of wedging of the dorsolumbar vertebral bodies, others may have a predisposition toward ruptured intervertebral discs. This is probably attributable to an inherent weakness in the spinal column of the achondroplastic dwarf.

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NOTICES

AMERICAN BOARD OF NEUROLOGICAL SURGERY

Examinations were given by the American Board of Neurological Surgery, September 19–21, 1952, in New Haven, Connecticut, and the following were certified

ALBERNAZ, JOSÉ GERALDO (foreign certificate) Instituto Neuro-Psiquiatrico Raul Soares, Belo Horizonte, Brazil
AUSTIN, GEORGE M. University Hospital, 34th & Spruce Sts., Philadelphia 4, Penna.
BALDWIN, MAITLAND 4200 East 9th Ave., Denver, Colo.
BERKAY, FEYYAZ M. Dept. of Surgery, University of Istanbul, Istanbul, Turkey
BLACK, SAMUEL P. W. 789 Howard Ave., New Haven 4, Conn.
CASTILLO, RAFAEL Centro Medico, Caracas, Venezuela
FREEDMAN, HOWARD 200 Hicks St., Brooklyn 2, N. Y.
GARRITY, RICHARD WILLIAM 4753 Rolando Blvd., San Diego, Calif.
GOGELA, LOUIS JAMES 1318 Sharp Bldg., Lincoln, Neb.
GRANGER, GEORGE R. 705 David Whitney Bldg., Detroit 26, Mich.
HILLIER, WILLIAM FRANCIS, JR. City Bldg., Asheville, N. C.
HUFF, THOMAS J., JR. 129 Osler Bldg., 1200 N. Walker, Oklahoma City, Okla.
JAMES, WILLIAM JOHN U. S. Naval Hospital, Chelsea 50, Mass.
JEFFREYS, EVERETT OSBOURNE 705–708 O'Hanlen Bldg., Winston-Salem, N. C.
KINAL, MURL E. 236 West 8th St., Erie, Penna.
LA LONDE, ALBERT AENEAS 806 Capital National Bank Bldg., Austin, Texas
LEWIS, REVIS C. 411 Nicholas Road, Kansas City 2, Mo.
MARSHALL, THOMAS MILTON Heyburn Bldg., Louisville 2, Ky.
MCCLINTOCK, HOMER GLENN 1809 East 18th Ave., Denver, Colo.
PACE, JOHN WILLIAM 1308 Olive Ave., Fresno 4, Calif.
PAGE, W. RANDOLPH 4900 St. Charles Ave., New Orleans, La.
PAGET, JOHN FRANCIS 270 Commonwealth Ave., Boston 16, Mass.
ROSENBERG, MEYER 61 Eastern Parkway, Brooklyn, N. Y.
SCHULTZ, ARTHUR LENTON U. S. Navy
*SPICER, CHARLES 812 Pine Ave., Long Beach 13, Calif.
TYRER, AUSTIN ROY, JR. 22 North Manassas, Memphis 5, Tenn.
WILSON, CHARLES M. 510 Medical Arts Bldg., Dallas, Texas
WINOKUR, GERALD L. 681 Bergen Ave., Jersey City, N. J.

The new Secretary of the Board is Dr. Leonard T. Furlow, Department of Surgery, Washington University School of Medicine, St. Louis 10, Missouri.

SOUTH AMERICAN CONGRESS OF NEUROSURGERY

The Fifth South American Congress of Neurosurgery will meet in Lima, Peru, at the Hospital Obrero, April 12–18, 1953. The main subjects to be presented are: (1) Pre- and postoperative care; (2) Blastomas of the posterior fossae; and (3) Surgical intracranial vascular lesions.

Neurosurgeons from other countries are welcome to attend the Congress. Information concerning hotel accommodations, etc. may be obtained by writing Dr. Esteban D. Rocca at the Hospital Obrero, Lima.

* Certified October, 1952.

INDEX TO VOLUME IX

Abbott, K. H., Gay, J. R., and Goodall, R. J. Clinical complications of cerebral angiography, 258
Adamantinoma present at birth, 221
Adson, Alfred Washington, 117
Aird, R. B., Strait, L. S., Zealear, D., and Hrenoff, M. Neurophysiological studies on cerebral concussion, 331
American Board of Neurological Surgery, 111, 420, 652
American Electroencephalographic Society, 233, 420
American Neurological Association, 111, 315, 420
von Amerongen, F. K. See French, J. D., 378
Aneurysm, intracranial
  bleeding, with subdural hematoma, 443
  of anomalous ophthalmic artery simulating aneurysm of internal carotid, 544
Angina pectoris, operation for relief of pain in, 197
Angiography, cerebral
  aneurysm of anomalous ophthalmic artery simulating aneurysm of internal carotid, 544
  carotid, ocular complications of, 517
  clinical complications of, 258
  effects of intracarotid diodrast, 68
  in children, 235
  radio-opaque screen for, 107
  transient loss of vision following, 547
Angioreticulomas, cerebellar, 317
Apparatus: See also Instruments
  bed attachment for head traction, 417
  device for position determination in myelography, 108
  radio-opaque screen for angiography, 107
Association for Research in Nervous and Mental Disease, 233, 553

Bailey, O. T., Ingraham, F. D., Weadon, P. S., and Susen, A. F. Tissue reactions to powdered tantalum in the central nervous system, 83
——, Small, W. T., and Ingraham, F. D. Procaine block of frontal lobe white fibers as a means of predicting the effect of prefrontal lobotomy. I. Experimental studies. With an introductory note by W. P. Van Wagenen, 21
Balyeat, G. W. See List, C. F., 177
Barrie, H. J. See Tonning, H. O., 124
Bassett, R. C., and Lemmen, L. J. Subdural hematoma associated with bleeding intracranial aneurysm, 443
Beller, A. J., and Peyser, E. Extradural cerebellar hematoma. Report of three cases with review of the literature, 291
Bering, E. A., Jr. Water exchange of central nervous system and cerebrospinal fluid, 275
Blood vessels: See also Aneurysm
  internal carotid artery thrombosis, ocular signs of, 517
  internal carotid artery thrombosis secondary to nonpenetrating injuries to neck, 495
Botterell, E. H., and Drake, C. G. Localized encephalitis, brain abscess and subdural empyema. 1945–1950, 348
Bouslog, J. S. See Murphy, E. S., 214
Brain
  concussion, neurophysiological studies on, 331
  cyst treated by intraventricular drainage, 219
  decerebrate state with supratentorial lesions, recovery from, 52
  effects of intracarotid nitrogen mustard on, 378
  electrical excitability of human motor cortex, 461
  localized encephalitis, abscess and subdural empyema, 348
  orbitofrontal lobotomy, effects of, on 55 psychotic patients, 579
  prefrontal lobotomy, procaine block as means of predicting effect of, 21, 30
  schistosomiasis of, 620
  torulosis of, 307
Brain injury: See Cranium; Head injury
Brain tumor: See Intracranial tumor
Bucy, P. C. Our training programs and the future of neurological surgery, 538
——, and Freeman, L. W. Hypertrophic spinal pachymeningitis with special reference to appropriate surgical treatment, 564

Calcinosis, tumoral, sciatica caused by, 304
Canadian Neurological Society, 233
Carmichael, F. A., Jr., and Cowley, H. S. Schistosomiasis of the brain, 620
Castellano, F., Guidetti, B., and Olivecrona, H. Pterional meningiomas "en plaque," 188
Cerebrospinal fluid
  and water exchange of central nervous system, 275
  overproduction of, and hydrocephalus, 59
Cerebrum: See Brain
Childe, A. E. See Parkinson, D., 404
Chipault, Antony, 299
Chordoma, 139
Chou, S. N. See Peyton, W. T., 432
Clark, G. The lucite calvarium. A case report, 103
Clark, R. A., Jr. See Negrin, J., Jr., 95
Clayton, C. F. Bed attachment for improved head traction, 417
Cloward, R. B. A self-retaining spinal dura retractor, 230
Colloid cyst of 4th ventricle, 404

Congress of Neurological Surgeons, 553
Cook, A. W., and Druckemiller, W. H. Phantom limb in paraplegic patients. Report of two cases and an analysis of its mechanism, 508
Cowley, H. S. See Carmichael, F. A., Jr., 620
Craig, W. McK. Alfred Washington Adson—pioneer neurosurgeon. 1887–1951, 117
See Johnson, D. A., 599
Cranium: See also Head injury
comparison of polyethylene and tantalum for cranioplasty, 254
erosion of, with chronic subdural hematoma, 639
lucite calvarium, 103
refrigerated autogenous bone flaps for cranioplasty, 606
tantalum cranioplasty and repeated trauma, 100
Crawford, A. S. Double-jointed tantalum-clip-applying forceps, 551
Cuneo, H. M., and Rand, C. W. Tumors of the Gasserian ganglion. Tumor of the left Gasserian ganglion associated with enlargement of the mandibular nerve. A review of the literature and case report, 423

Davis, L., Martin, J., and Goldstein, S. L. Sensory changes with herniated nucleus pulposus, 133
Dodge, P. R., and Meirowsky, A. M. Tangential wounds of scalp and skull, 472
Drake, C. G. See Botterell, E. H., 348
Druckemiller, W. H. See Cook, A. W., 508
Duisberg, R. E. H. See Green, J. R., 579

Ecker, A. See Riemenschneider, P. A., 304
See Taheri, Z. E., 93
Electroencephalography in subdural hematoma, 588
Embolism, fat, in diagnosis of craniocerebral trauma, 1

Foltz, E. L., Thomas, L. B., and Ward, A. A., Jr. The effects of intracarotid diodrast, 68
Freedman, H. Recovery from the decerebrate state associated with supratentorial space-taking lesions, 52
Freeman, L. W. See Bucy, P. C., 564
French, J. D. See Trowbridge, W. V., 398, 643
——, West, P. M., von Ameron gen, F. K., and Magoun, H. W. Effects of intracarotid administration of nitrogen mustard on normal brain and brain tumors, 378
French, L. A. See Peyton, W. T., 432

Gay, J. R. See Abbott, K. H., 258
Gish, G. R., Jr. See Meredith, J. M., 639
Gliomatosis cerebri, 409
Glusman, M., Ransohoff, J., Pool, J. L., Grundfest, H., and Mettler, F. A. Electrical excitability of the human motor cortex. I. The parameters of the electrical stimulus, 461
Goldstein, S. L. See Davis, L., 133
González-Revilla, A. Intracranial tuberculomas. Experience with ten consecutive cases, 555
Goodall, R. J. See Abbott, K. H., 258
Grantham, E. G., and Segerberg, L. H. An evaluation of palliative surgical procedures in trigeminal neuralgia, 390
Green, J. R., Duisberg, R. E. H., and McGrath, W. B. Orbitofrontal lobotomy with reference to effects on 55 psychotic patients, 579
Greenberg, I. M. A simple device for position determination during myelography, 108
Greenwood, J., Jr., McGuire, T. H., and Kimbell, F. A study of the causes of failure in the herniated intervertebral disc operation. An analysis of sixty-seven reoperated cases, 15
Groff, R. A. See Lockhart, W. S., Jr., 254
Grundfest, H. See Glusman, M., 461
Guidetti, B. See Castellano, F., 188

Harvey Cushing Society, 114, 421
Head injury: See also Cranium
differential diagnosis from nonpenetrating injuries to neck, 495
fat embolism in diagnosis of, 1
tangential wounds of scalp and skull, 472
Hemangioma
cerebellar, familial, 124
cerebellar, review of 40 cases, 484
Hematoma
chronic subdural, producing erosion of skull, 639
extradural cerebellar, 291
extradural, of posterior fossa, 245
subdural, electroencephalogram in, 588
subdural, with bleeding intracranial aneurysm, 443
Hennigar, G. See Silver, M. L., 484
Hrenoff, M. See Aird, R. B., 331
Hydrocephalus
from overproduction of cerebrospinal fluid, 59
nonobstructive, treatment of, 164

Ingraham, F. D. See Bailey, O. T., 21, 83
Instruments: See also Apparatus
double-jointed tantalum-clip-applying forceps, 551
spinal dura retractor, 230
International Congress of Neuropathology, 111
International Neurological Congress, 112
Intervertebral disc, herniated
causes of failure in operation for, 15
lumbar, 229
lumbar, paraplegia from, in achondroplastic dwarfs, 648

sensory changes with, 133
Intracranial tumor
adamantinoma present at birth, 221
angioreticulomas, cerebellar, 317
arachnoid cysts, benign, of posterior fossa, 398
chordoma, 13 cases, 139
colloid cyst of 4th ventricle, 404
cyst, cerebral, treated by intraventricular drainage, 219
decerebrate state with, 52
effects of intracarotid nitrogen mustard on, 378
Gasserian ganglion tumors, 423
gliomatosis cerebri, 409
hemangioma, cerebellar, familial, 124
hemangioma, cerebellar, 40 cases, 484
meningiomas, pterional "en plaque," 188
neutron-capturing isotopes in treatment of, 200
oligodendroglioma, disseminated, 643
papillomas of choroid plexus, 59
paragasserian, 451
pituitary adenomas, vascular lesions in, 177, 210
radioactive isotopes in localization of, 432
tuberculomas, 10 cases, 555
unilateral acoustic, unusual case of, 395
Iyer, C. G. S. Case report of an adamantinoma present at birth, 221

Javid, M. See Sweet, W. H., 200
Johnson, D. A., Roth, G. M., and Craig, W. McK. Autonomic pathways in the spinal cord, 599
Jones, O. W., Jr. See Malamud, N., 409

Kahn, E. A., and Luros, J. T. Hydrocephalus from overproduction of cerebrospinal fluid (and experiences with other papillomas of the choroid plexus), 59
——, and Rand, R. W. On the anatomy of anterolateral cordotomy, 611
Kimbell, F. See Greenwood, J., Jr., 15
Kimsey, W. H. See Lockhart, W. S., Jr., 254
King, A. B. See Poppen, J. L., 139
Kinley, G. J., and Leighninger, D. S. Aneurysm of anomalous ophthalmic artery presenting in the sphenoid sinus and simulating an aneurysm of the internal carotid artery on routine arteriography, 544

Lehnert, H. B. See Schnitker, M. T., 210
Leighninger, D. S. See Kinley, G. J., 544
Lemmen, L. J. See Bassett, R. C., 443
See Schneider, R. C., 495
——, and Schneider, R. C. Extradural hematomas of the posterior fossa, 245
Levy, L. L., Segerberg, L. H., Schmidt, R. P., Turrell, R. C., and Roseman, E. The electroencephalogram in subdural hematoma, 588
Lipscomb, W. R. See Murphy, E. S., 214
List, C. F., Williams, J. R., and Balyeat, G. W. Vascular lesions in pituitary adenomas, 177
Liu, C. T. See Van Wagenen, W. P., 30
Lobotomy: See Brain
Lockhart, W. S., Jr., van den Noort, G., Kimsey, W. H., and Groff, R. A. A comparison of polyethylene and tantalum for cranioplasty. A preliminary report, 254
Lucite calvarium, 103
Luros, J. T. See Kahn, E. A., 59

McEachern, D. Lumbar disc protrusion, 229
McGrath, W. B. See Green, J. R., 579
McGuire, T. H. See Greenwood, J., Jr., 15
Magoun, H. W. See French, J. D., 378
Malamud, N., Wise, B. L., and Jones, O. W., Jr. Gliomatosis cerebri, 409
Marie, Pierre, centenaire de, 315
Mark, V. H., and Sweet, W. H. An unusual case of unilateral eighth nerve tumor, 395
Markham, J. See Otenasek, F. J., 547
Martin, J. See Davis, L., 133
See Padberg, F., 307
Meirowsky, A. M. See Dodge, P. R., 472
Meninges
arachnoid cysts, benign, of posterior fossa, 398
pachymeningitis, hypertrophic spinal, 564
spinal, subdural abscess of, 95
subdural empyema, 348
Meningiomas
multiple, of spinal cord, 310
pterional "en plaque," 188
Meredith, J. M., and Gish, G. R., Jr. Chronic subdural hematoma in an adult producing marked erosion and perforation of the overlying dura and skull. Report of case with operation and recovery, 639
Mettler, F. A. See Glusman, M., 461
Miller, D. Cyst of a cerebral hemisphere treated by intraventricular drainage, 219
Moore, G. E. See Peyton, W. T., 432
Murphy, E. S., Lipscomb, W. R., and Bouslog, J. S. Neurogenic sarcoma treated by surgery and radiotherapy, 214
Myelography
device for position determination in, 108
diagnosis of sacral perineurial cyst, 93

National Paraplegia Foundation, 234
Neck injury, nonpenetrating, internal carotid artery thrombosis secondary to, 495
Negrin, J., Jr., and Clark, R. A., Jr. Pyogenic subdural abscess of the spinal meninges. Report of two cases, 95
Nerve: See also Paralysis
Gasserian ganglion, tumors of, 423
neurogenic sarcoma treated by surgery and radiotherapy, 214
sciatica caused by tumoral calcinosis, 304
trigeminal neuralgia, palliative surgery in, 390

trigeminal neuralgia, review of 689 cases, 367
trigeminal neuralgia, treatment of, by decompression of root and ganglion, 288
Nervous system
sensory changes with herniated nucleus pulposus, 133
tissue reactions to powdered tantalum, 83
water exchange of, and cerebrospinal fluid, 275
Neurinoma, acoustic, unusual case of, 395
Neurosurgery: See also Apparatus; Instruments
neurologist in world of, 635
training programs and future of, 538
Neurosurgical societies
Harvey Cushing Society, 114, 421
Neurosurgical Society of America, 114, 421
New York Society of Neurosurgery, 234, 553
Scandinavian Neurosurgical Society, 315
Neurosurgical Society of America, 114, 421
New York Society of Neurosurgery, 234, 553
Nitrogen mustard, effects of intracarotid administration of, on normal brain and tumors, 378
VAN DEN NOORT, G. See Lockhart, W. S., Jr., 254

ODOM, G. L., WOODHALL, B., and WRENN, F. R., JR. The use of refrigerated autogenous bone flaps for cranioplasty, 606
Oligodendroglioma, disseminated, 643
OLIVECRONA, H. The cerebellar angioreticulomas, 317
See Castellano, F., 188
OTENASEK, F. J., and MARKHAM, J. Transient loss of vision following cerebral arteriography, 547

PADBERG, F., and MARTIN, J. Torulosis of the brain. A case report, 307
Papillomas of choroid plexus and hydrocephalus, 59
Paralysis
paraplegia from ruptured lumbar discs in achondroplastic dwarfs, 648
phantom limb in paraplegic patients, 508
PARKINSON, D., and CHILDE, A. E. Colloid cyst of the fourth ventricle. Report of a case of two colloid cysts of the fourth ventricle, 404
PEET, M. M., and SCHNEIDER, R. C. Trigeminal neuralgia. A review of six hundred and eighty-nine cases with a follow-up study on sixty-five per cent of the group, 367
PETIT-DUTAILLIS, D. Antony Chipault. 1866–1920, 299
PEYSER, E. See Beller, A. J., 291
PEYTON, W. T., MOORE, G. E., FRENCH, L. A., and CHOU, S. N. Localization of intracranial lesions by radioactive isotopes, 432
Phantom limb in paraplegic patients, 508
PICAZA, J. A. Cerebral angiography in children. An anatomoclinical evaluation, 235
Pituitary adenomas
apoplexy in, producing syndrome of middle cerebral artery thrombosis, 210
vascular lesions in, 177
Polyethylene compared with tantalum for cranioplasty, 254
POOL, J. L. See Glusman, M., 461
POPPEN, J. L., and KING, A. B. Chordoma: experience with thirteen cases, 139

Radioactivity
isotopes in localization of lesions, 432
neutron-capturing isotopes in treatment of neoplasms, 200
RAND, C. W. See Cuneo, H. M., 423
RAND, R. W. Multiple spinal cord meningiomas, 310
See Kahn, E. A., 611
RANSOHOFF, J. See Glusman, M., 461
RIEMENSCHNEIDER, P. See Taheri, Z. E., 93
——, and ECKER, A. Sciatica caused by tumoral calcinosis. A case report, 304
ROBSON, J. T. A new operation for the relief of pain in angina pectoris, 197
Roentgenology: See Angiography
ROSEMAN, E. See Levy, L. L., 588
ROSENTHAL, H. See Schreiber, F., 648
ROTH, G. M. See Johnson, D. A., 599

Sarcoma, neurogenic, treated by surgery and radiotherapy, 214
Scandinavian Neurosurgical Society, 315
SCARFF, J. E. Nonobstructive hydrocephalus. Treatment by endoscopic cauterization of the choroid plexus. Long term results, 164
Schistosomiasis of brain, 620
SCHMIDT, R. P. See Levy, L. L., 588
SCHNEIDER, R. C. Fat embolism. A problem in the differential diagnosis of craniocerebral trauma, 1
See Lemmen, L. J., 245
See Peet, M. M., 367
——, and LEMMEN, L. J. Traumatic internal carotid artery thrombosis secondary to nonpenetrating injuries to the neck. A problem in the differential diagnosis of craniocerebral trauma, 495
SCHNITKER, M. T., and LEHNERT, H. B. Apoplexy in a pituitary chromophobe adenoma producing the syndrome of middle cerebral artery thrombosis. Case report, 210
SCHREIBER, F., and ROSENTHAL, H. Paraplegia from ruptured lumbar discs in achondroplastic dwarfs, 648
SEGERBERG, L. H. See Grantham, E. G., 390
See Levy, L. L., 588
SILVER, M. L., and HENNIGAR, G. Cerebellar hemangioma (hemangioblastoma). A clinicopathological review of 40 cases, 484
Skull: See Cranium
SMALL, W. T. See Bailey, O. T., 21
SMILEY, G. L. A simple radio-opaque screen for angiography, 107
SMITH, G. W. See Walsh, F. B., 517
South American Congress of Neurosurgery, 652

Spinal cord
anatomy of anterolateral cordotomy, 611
autonomic pathways in, 599
multiple meningiomas of, 310
Spine: See also Intervertebral disc
hypertrophic pachymeningitis of, 564
sacral perineurial cyst, myelographic diagnosis of, 93
subdural abscess of spinal meninges, 95
SPRAIT, L. S. See Aird, R. B., 331
SVEN, A. F. See Bailey, O. T., 83
SWEET, W. H. See Mark, V. H., 395
——, and JAVID, M. The possible use of neutron-capturing isotopes such as Boron[10] in the treatment of neoplasms. 1. Intracranial tumors, 200
Symposium Neuroradiologicum, 315

THAARNHØJ, P. Decompression of the trigeminal root and the posterior part of the ganglion as treatment in trigeminal neuralgia. Preliminary communication, 288
TAHERI, Z. E., RIEMENSCHNEIDER, P., and ECKER, A. Myelographic diagnosis of sacral perineurial cyst, 93
Tantalum
compared with polyethylene for cranioplasty, 254
cranioplasty and repeated trauma, 100
powdered, tissue reactions to, in central nervous system, 83
THOMAS, L. B. See Foltz, E. L., 68
TONNING, H. O., WARREN, R. F., and BARRIE, H. J. Familial haemangiomata of the cerebellum. Report of three cases in a family of four, 124
Torulosis of brain, 307
TROWBRIDGE, W. V., and FRENCH, J. D. Benign arachnoid cysts of the posterior fossa, 398
Disseminated oligodendroglioma, 643
Tuberculomas, intracranial, 555
TURNER, O. A. Tantalum cranioplasty and repeated trauma, 100
TURRELL, R. C. See Levy, L. L., 588

VAN WAGENEN, W. P. See Bailey, O. T., 21
——, and LIU, C. T. Procaine block of frontal lobe white fibers as a means of predicting the effect of prefrontal lobotomy. II. Clinical evaluation, 30
VER BRUGGHEN, A. Paragasserian tumours, 451
Vision, transient loss of, following cerebral arteriography, 547

WALSH, F. B., and SMITH, G. W. The ocular complications of carotid angiography. The ocular signs of thrombosis of the internal carotid artery, 517
WARD, A. A., JR. See Foltz, E. L., 68
WARREN, R. F. See Tonning, H. O., 124
WEADON, P. S. See Bailey, O. T., 83
WEST, P. M. See French, J. D., 378
WILLIAMS, J. R. See List, C. F., 177
WISE, B. L. See Malamud, N., 409
WOODHALL, B. See Odom, G. L., 606
WRENN, F. R., JR. See Odom, G. L., 606

YASKIN, J. C. Is there room for a neurologist in a neurosurgical world, 635

ZEALEAR, D. See Aird, R. B., 331